

The effect of diet and physical activity on quality of life, wellbeing and treatment satisfaction, in newly diagnosed Type 2 diabetes

MSc by Research, Medical Studies

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Abstract

Type 2 diabetes impacts upon quality of life. Quality of life is lower in diabetes than in the general population but what happens to quality of life over the first years following the diagnosis is less clear. In addition, Type 2 diabetes is associated with depression and other psychological problems.

Diet and physical activity are cornerstones of the management of diabetes. Despite the multitude of benefits these lifestyle changes have, adherence to these interventions is poor with people with Type 2 diabetes experiencing numerous barriers to dieting and exercising. A possible reason for the poor adherence could be that these interventions result in a reduction in quality of life or wellbeing, or reduced satisfaction with their treatment.

The aim of this thesis is determine the effects of diet and physical activity interventions on quality of life, wellbeing and treatment satisfaction in newly diagnosed Type 2 diabetes, as well as to explore what changes in quality of life and wellbeing occur in first years following diagnosis.

Chapter 1 reviews the current evidence of the changes in quality of life and wellbeing that occur in Type 2 diabetes over time, their associations and how they are effected by lifestyle interventions.

Chapter 2 describes the Early ACTvity in Diabetes randomised control trial of lifestyle interventions in early Type 2 diabetes from which the dataset originates.

Chapter 3 demonstrates lifestyle interventions delivered in newly diagnosed Type 2 diabetes improve treatment satisfaction and do not affect quality of life and wellbeing. It also demonstrates quality of life and wellbeing are not associated with response.

Chapter 4 demonstrates quality of life decline slowly over the first six years following diagnosis of Type 2 diabetes, and that this change is likely part of the normal progression of Type 2 diabetes. It also demonstrates wellbeing does not change over this period and that lifestyle interventions have no lasting effect on quality of life or wellbeing.

Chapter 5 brings together the main findings of this thesis and their clinical implications, and provides direction for future work.

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Abbreviations

ACTID Plus	Early ACTID Follow Up Study
ADA	American Diabetes Association
ADDQOL	Audit of Diabetes Quality of Life
BDI	Beck Depression Inventory
BIPQ	Brief Illness Perception Questionnaire
BMI	Body Mass Index
CONSORT	Consolidated Standards of Reporting Trials
DESMOND	Diabetes Education and Self-Management for Ongoing and Newly Diagnosed
DiRECT	Diabetes Remission Clinical Trial
DM	Diabetes Mellitus
DPP	Diabetes Prevention Program
DPP-IV	Dipeptidyl Peptidase-4
DPPOS	Diabetes Prevention Program Outcomes Study
DQOL	Diabetes Quality of Life Questionnaire
DSE	Diabetes Support and Education arm (of Look AHEAD)
DTSQ	Diabetes Treatment Satisfaction Questionnaire
DTSQc	Diabetes Treatment Satisfaction Questionnaire Change
Early ACTID	Early ACTivity in Diabetes Study
EQ-5D	EuroQoL – 5 Dimensions
GLP-1	Glucagon-Like Peptide-1
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HbA1c	HaemoglobinA1c/Glycosylated Haemoglobin
HCD	High Carbohydrate Diet
HDL	High-Density Lipoprotein
HOMA	Homeostatic Model Assessment
IDES	Italian Diabetes and Exercise Study
IDF	International Diabetes Federation
ILI	Intensive Lifestyle Intervention Arm (of Look AHEAD)
ILS	Intensive Lifestyle Intervention Arm (of DPP)
IPQ	Illness Perception Questionnaire

IQR	Inter-Quartile Range
LCD	Low Carbohydrate Diet
LDL	Low-Density Lipoprotein
Look AHEAD	Action for Health in Diabetes
MCS	Mental Component Summary (of SF-36)
MET	Metformin Treatment Arm (of DPP)
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPH	Neutral protamine Hagedorn
PAID	Problem Areas In Diabetes Questionnaire
PARQ	Physical Activity Readiness Questionnaire
PCS	Physical Component Summary
PLB	Placebo arm (of DPP)
RCT	Randomised Controlled Trial
RSES	Rosenberg Scale of Self-Esteem
SD	Standard Deviation
SF-36	Short Form – 36
SF-6D	Short Form – 6 Dimension
SGLT-2	Sodium-Glucose Cotransporter 2
SU	Sulphonylurea
SWLS	Satisfaction With Life Scale
TG	Triglycerides
UKPDS	United Kingdom Prospective Diabetes Study
VAS	Visual Analogue Scale
W-BQ 12	Well-being Questionnaire (12 items)
W-BQ 22	Well-being Questionnaire (22 items)
W-BQ 28	Well-being Questionnaire (28 items)
WHO	World Health Organisation
WHOQOL	WHO Quality of Life
WHOQOL-BREF	WHO Quality of Life Short Version

Introduction

This thesis is composed of five chapters.

Chapter 1 aims to provide a thorough background to the project with a review of relevant literature and description of the project's aims and hypotheses.

Chapter 2 aims to provide an overview of the Early ACTivity In Diabetes (Early ACTID) randomised control trial; the study that provides the data for this project. It will use the CONSORT guidance as a framework and provide more in-depth information on the questionnaires used.

Chapter 3 aims to assess the impact of diet and diet and physical activity interventions on treatment satisfaction, quality of life, illness perception and wellbeing in newly diagnosed Type 2 diabetes using data from the Early ACTID randomised control trial.

Chapter 4 aims to assess the long-term impact of lifestyle interventions on treatment satisfaction, quality of life, illness perception and wellbeing over up to five years following completion of the Early ACTID trial using data from the follow up study ACTID Plus. It will also aim to assess the changes that occur over time in quality of life, illness perception and wellbeing over the first 6 years following diagnosis of Type 2 diabetes in this cohort.

Chapter 5 aims to discuss the principal findings of this project, where they fit with current literature, their implications, and future directions for research in this field.

Chapter 1 - Background

1.1 Type 2 diabetes

1.1.1 Definition

Type 2 diabetes is a disease of high blood glucose due to a combination of pancreatic beta cell dysfunction and insulin resistance in target organs (1). It is characterised by hyperinsulinaemia, insulin resistance and eventual beta cell failure. On the other hand, Type 1 diabetes is an autoimmune destruction of the pancreatic beta cells leading to severe insulin deficiency. The distinction between Type 1 and Type 2 diabetes was made as early as 500-600 BC by Sushruta and Charaka. Type 1 was described as the diabetes of youth and Type 2 was the diabetes of obesity (2). To this day, Type 2 diabetes is more common at older ages and Type 1 diabetes is mainly considered a disease of childhood. However, increasing obesity and better identification of Type 1 diabetes in older adults means this distinction is more blurred than previously thought (3). Type 2 diabetes accounts for 90% of all diabetes, is on the rise, and comes with complications that result in significant morbidity and mortality (4).

1.1.2 Epidemiology

Type 2 diabetes is a growing problem worldwide, with the final quarter of the 20th century seeing the incidence and prevalence of Type 2 diabetes quadruple. The estimated global prevalence for adults between the ages of 20-70 in 2017 is 1 in 11 (425 million), with 1 in 2 of these people undiagnosed. The major contributing factors to this increase are thought to be calorie-rich diets and increasingly sedentary lifestyles (4).

1.1.3 Pathophysiology

Fundamentally the hyperglycaemia of Type 2 diabetes is the result of dysregulation of the feedback loop involving beta-cells and insulin sensitive tissues (Figure 1).

Stimulation of beta-cells results in the release of insulin. Insulin acts on insulin-sensitive tissues to mediate the uptake of glucose, amino acids and fatty acids, thus reducing blood glucose. The insulin-sensitive tissues then feedback their insulin requirement to the beta-cells by a hitherto unknown mechanism. If insulin resistance is present, beta-cells increase production of insulin to

increase uptake of glucose to return to euglycaemia. However, if these beta-cells are unable sufficiently increase insulin production in response to this, the hyperglycaemic state persists (5).

The reasons behind the development of this dysregulation are likely to be a combination of genetic and environmental factors (Figure 2). At the moment the insulin resistance caused by obesity accounts for up to 80% of Type 2 diabetes, and the development of insulin resistance as a result of obesity is thought to progress more rapidly to Type 2 diabetes in those with genetic risk for beta-cell dysfunction (4,5).

1.1.4 Complications

Persistent hyperglycaemia leads to severe microvascular and macrovascular complications. Microvascular complications include retinopathy that can lead to blindness, nephropathy that can lead to renal failure, and peripheral neuropathy that can lead to severe motor, sensory and autonomic dysfunction. Retinopathy affects 20 per cent of people with Type 2 diabetes and across all of forms of diabetes is responsible for 1280 new cases of blindness every year (6,7).

Nephropathy accounts for 11% of deaths in people with Type 2 diabetes (8).

Neuropathy is common across all types of diabetes and leads to 7000 diabetes related amputations each year in the UK (9). In addition, up to 80% of people having amputations die within five years (10). Improving glycaemic control significantly reduces the rates of these microvascular complications (1).

Cardiovascular disease is the major macrovascular complication of diabetes. A large scale meta-analysis showed the presence of diabetes doubled the risk of coronary heart disease, more than doubled the risk of ischaemic stroke and increased the risk of death from other vascular disease by 73% (11). However, it is less clear what impact improved glycaemic control has on macrovascular complications.

Despite improved knowledge and treatment of Type 2 diabetes its complications are still responsible for huge morbidity and mortality. Treatment of diabetes related complications cost healthcare systems vast sums of money, with diabetes-related foot ulcers and amputations costing £1 of every £140 spent on the NHS (9).

Figure 1 – *Dysregulation of glucose homeostasis by beta-cells and insulin-sensitive tissues. (A) Normal blood glucose levels maintained by action of insulin on insulin-sensitive tissues. The amount of insulin produced is determined by the insulin sensitivity of target tissues. (B) Insulin resistance in insulin-sensitive tissues leads to increased insulin production by beta-cells but normal blood glucose levels are maintained. (C) Beta-cells unable to produce sufficient insulin in response to insulin resistance in target tissues. This leads to inadequate glucose uptake and high blood glucose levels. Image taken from Kahn et al. (5)*

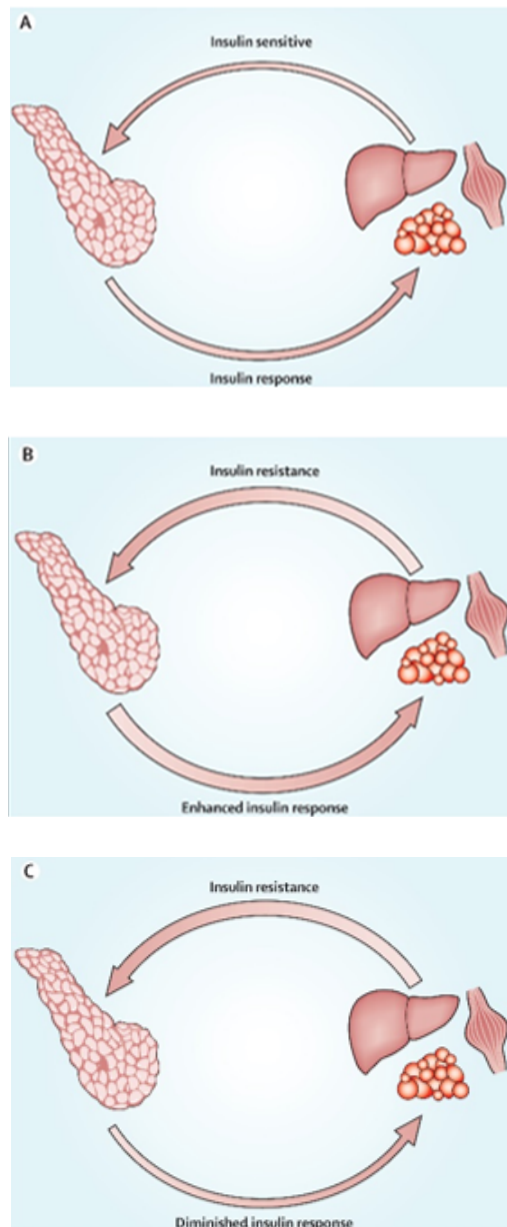
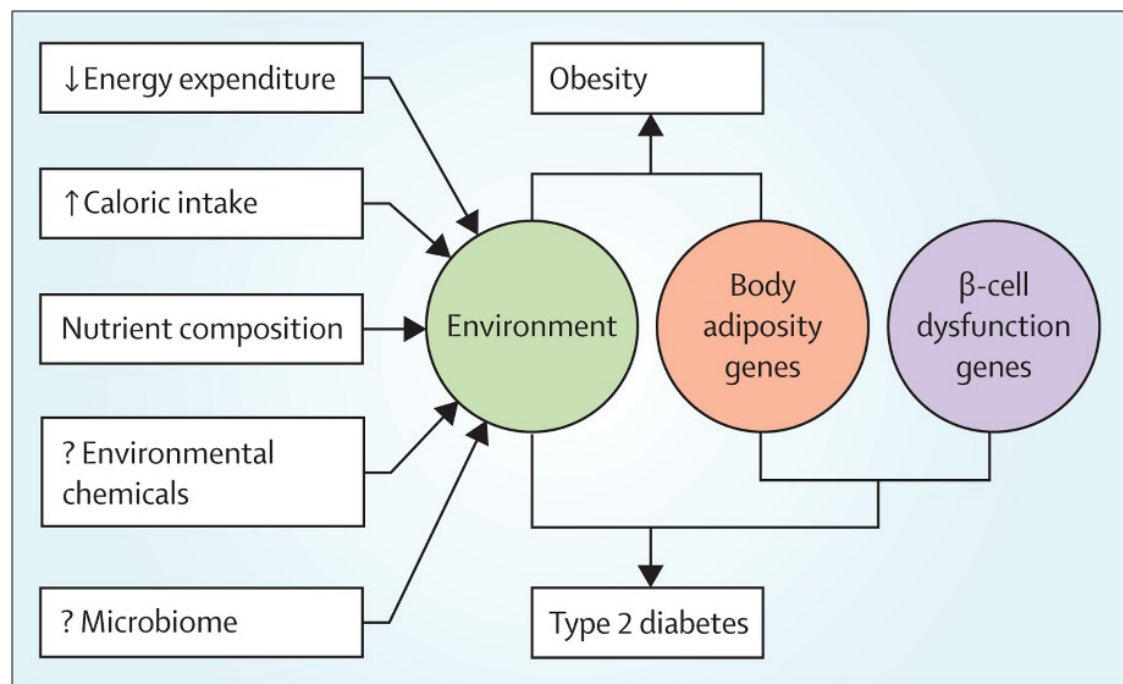


Figure 2 – Factors leading to the development of obesity and Type 2 diabetes.
Taken from Kahn et al. (5)



1.1.5 Treatment

Type 2 diabetes is managed by a combination of diet, exercise and pharmacological therapies (Figure 3). The first step is to give general diet and activity advice. In the UK, this is often given in primary care, soon after diagnosis. Diet and physical activity are the cornerstone of diabetes prevention and management. With obesity underlying 80% of cases of Type 2 diabetes it makes sense that lifestyle changes resulting in weight loss are effective in both preventing and treating Type 2 diabetes. Lifestyle changes have been shown conclusively to prevent the development of diabetes in those with impaired glucose tolerance (12,13). In those with Type 2 diabetes, lifestyle changes reduce body weight, improve glycaemia, insulin sensitivity, blood pressure, lipids, endothelial function and may improve morbidity and mortality (14–21). Considerable weight loss through intensive dietary interventions has even been shown to achieve diabetes remission in overweight people with Type 2 diabetes (22).

Adherence to lifestyle changes in Type 2 Diabetees is poor. The recent Time2DoMore survey showed adherence to dietary changes was just 51% and adherence to physical activity advice 40%. This was a multinational survey of 652 adults with diabetes and 337 treating physicians assessing clinical inertia in diabetes treatment. With this in mind an increasing body of work is looking at the barriers preventing patients from adhering to lifestyle interventions (23).

This work revealed lifestyle changes are a significant burden for patients. A survey of US patients found moderate dietary changes to be a greater burden than oral glucose lowering agents. Furthermore, strict dietary changes were rated as equally burdensome to insulin therapy. Focus groups in this study cited reasons such as cost, small portion sizes and quality of life/lifestyle issues (24). Encouraging people to increase their physical activity, particularly in those who are most sedentary is just as troublesome. Sweating and physical discomfort were the main barriers identified by a 2009 systematic review. In addition, the feeling of being too fat to exercise was common and in keeping with this, adults of normal weight experience fewer barriers to exercise (25).

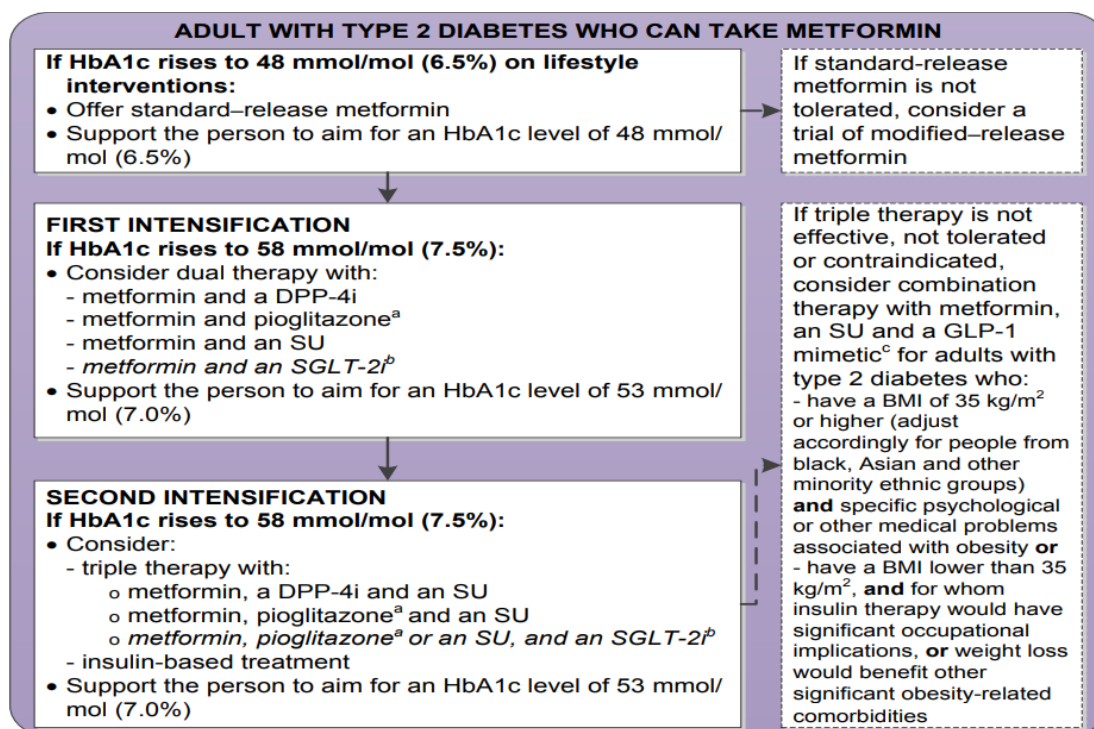
The next step is medical therapy with metformin, it reduces hepatic glucose output, improves insulin sensitivity, and stimulates GLP-1 secretion. Importantly,

it is also weight neutral and lowers HbA1c by around 10-20 mmol/mol. No single drug has been identified as the optimum second line treatment, as the current advice is to add one of any of the following drug classes; sulfonylureas, DPP-IV inhibitors, SGLT-2 inhibitors, thiazolidinediones, or an injectable GLP-1 receptor agonist (26).

The main aim of treatment is to improve blood glucose control to prevent the development of complications. The key marker of blood glucose control in diabetes is glycosylated haemoglobin (HbA1c) as this is the most closely associated marker with complications in key studies (27,28). HbA1c is a measure of the proportion of haemoglobin which is glycated by glucose in the bloodstream. As the life of a red blood cell is around 12 weeks the measure provides evidence of the glycaemic status of the individual over the previous 3 months. An HbA1c level of 48mmol/mol (6.5%) or more is diagnostic of the disease, and patients may well be asymptomatic at this time. Those with an HbA1c level of 43-48mmol/mol are defined as having impaired glucose tolerance or 'prediabetes' and have a high risk of progressing to Type 2 diabetes. Therefore, HbA1c is the key outcome in clinical practice and in most interventional trials in diabetes.

Despite oral medical therapy, many people with Type 2 diabetes progress to requiring insulin treatment, which comes with an array of complications and carries a lot of stigma with patients. Insulin treatment requires patients to closely monitor their glucose levels, self-inject insulin, and carries the risk of hypoglycaemia. Fear of hypoglycaemia and worry about self-management and complications are common in insulin-treated patients (29). Therefore, avoiding progression to insulin therapy with effective early treatment through lifestyle changes is paramount.

Figure 3 – NICE Guideline for medical management of Type 2 diabetes.



1.2 Quality of Life

1.2.1 What is quality of life?

An individual's quality of life can be described as a global status of a person's perception of their own physical, mental, social and emotional wellbeing. As such, if you were to assess the quality of life of two people who objectively had an identical health status their quality of life could be different (30).

It can be argued that research based on patient-reported wellbeing, quality of life and satisfaction is more relevant to patients than any biomedical outcome. The WHO definition of health states that health is not only the absence of illness but instead a feeling of physical, mental and social wellbeing (31).

1.2.2 How is it measured?

Historically quality of life research has primarily been interview-based but increasingly it is reported using standardised questionnaires. These often have multiple domains answered on standardised scales, e.g. a Likert Scale from Strongly Agree to Strongly Disagree (32).

There are two basic approaches to assessing quality of life in this way. Some measures assess general quality of life and other assess disease-specific quality of life. Each approach comes with its own benefits. Generic measures have the advantage of being applicable across different diseases and giving a more complete view of an individual's quality of life, usually across numerous domains. Disease-specific measures have the advantage of assessing specific problems people with a particular disease may face. For example, in diabetes research the Diabetes Quality of Life (DQOL) questionnaire considers the impact of hypoglycaemia, self-monitoring of blood sugars, and self-injection of insulin (30,32).

Although quality of life is fundamentally the most important outcome for patients, doing research into it can be difficult. Results are subject to within-individual variation as well as between-individual variation. Furthermore, as quality of life is affected by so many factors is difficult to attribute causal relationships. However, disease-specific questionnaires make this easier by being more specific to the condition and its treatment.

It is also difficult to create a questionnaire that is reliable enough to return similar results in similar people but responsive enough to illustrate changes in quality of life at different times. For this reason, new questionnaires are validated in different populations to ensure their reliability as a research tool. It is also important to determine the clinical significance of changes in questionnaire scores. Knowing what degree of change in a particular questionnaire score represents a noticeable difference for that person in the real world is fundamental to assessing quality of life.

Many questionnaires that assess quality of life focus on an individual's health status. Health status can be defined as the presence of biological or psychological dysfunction, symptoms and functional status (33). For this reason they can fail to pick the impact of these other aspects of an individual's life and may under report differences in quality of life.

Evaluation of the psychometric properties of questionnaires is focused on two major properties; reliability and validity (34). Reliability (how repeatable the results are) can be assessed in numerous ways. The two most common ways reported are test-retest reliability and Cronbach's alpha of internal consistency. Test-retest reliability is simply the correlation between the results when the questionnaire is given to the same individuals on two separate occasions. Internal consistency measured using Cronbach's alpha is more complex. Cronbach's alpha is the degree to which the items of the questionnaire are correlated. The more similar the items the higher value of alpha. It is important to note the great influence the number of items has, with fewer items resulting in a lower value of alpha. A maximum value for alpha of 0.9 has therefore been advocated and a value higher than this suggests redundant items. As with reliability, there are numerous type of validity (how well the results represent the truth). The most commonly reported are construct validity and concurrent validity. Construct validity is the extent to which the questionnaire measures the intended psychological construct. Concurrent validity is the extent to which the results are correlated with similar questionnaires. For example, a measure of life satisfaction would be expected to correlate negatively with a questionnaire assessing depression.

Table 1 – *Description of popular patient-reported outcome measures used in diabetes. Adapted from Speight et al. (33)*

Measure	Description
Measures of Health Status	
EQ-5D	A generic measure that primarily assesses health status. Part one is a health index created from five items: Mobility, Self-Care, Pain, Usual activities, and Anxiety/depression. Part two is a visual analogue scale used to indicate an individual's overall perception of their health.
SF-36	A generic measure of health status. Composed of 36 items and reported as 8 domains: Bodily Pain, Mental Health, Role-emotional, Role-physical, physical functioning, social functioning, vitality, and general health.
Generic measures of quality of life	
WHOQOL	Generic measure of quality of life composed of 100 items assessing 25 different aspects of quality of life across themes including physical, psychological, social and emotional quality of life.
WHOQOL-BREF	Shortened version of WHOQOL, Composed of 26 items that are reported on four subscales: physical health, psychological health, social relationships, and environment. Two items assess overall quality of life and general health.
Diabetes specific measures of quality of life	
ADDQOL	ADDQOL is a diabetes specific measure of quality of life. It is made up of 18 items. Scores are weighted according to which domains an individual feels are most important. Covers various aspects of quality of life including; working life, social life, family life, sex life holidays and leisure, and enjoyment of food. Two summary items measure current quality of life and diabetes-dependent quality of life.
DQOL	The first measure of diabetes specific quality of life developed for use in the Diabetes Control and Complications Trial (DCCT). Composed of four subscales that measure satisfaction, impact, social worry and diabetes worry.
Measures of wellbeing	
BDI	The Beck Depression Inventory is composed of 21 items. Each item is a list of four statements arranged in increasing severity about a particular symptom of depression, including biological symptoms.
HADS	Hospital Anxiety and Depression Scale is composed of 14 items: 7 assess depression and 7 assess anxiety
PAID	A diabetes specific measure of emotional distress caused by diabetes and its treatment composed of 20 items.
W-BQ 12	A generic measure of psychological wellbeing. 12 items are scored on 3 subscales of positive wellbeing, negative wellbeing and energy.
W-BQ 28	A measure of generic and disease specific psychological wellbeing. 28 items are scored on 7 subscales; 3 assess diabetes specific positive wellbeing, negative wellbeing, and stress; the other 4 assess general positive wellbeing, negative wellbeing, energy and stress.
Measures of treatment satisfaction	
DTSQ	A diabetes specific measure of treatment satisfaction. Composed of 8 items; six assess satisfaction. This covers: satisfaction, convenience, flexibility, understanding, likelihood of recommending, likelihood of continuing. The remaining two items assess perceived frequency of hypo/hyperglycaemia

1.2.3 How is it measured in diabetes?

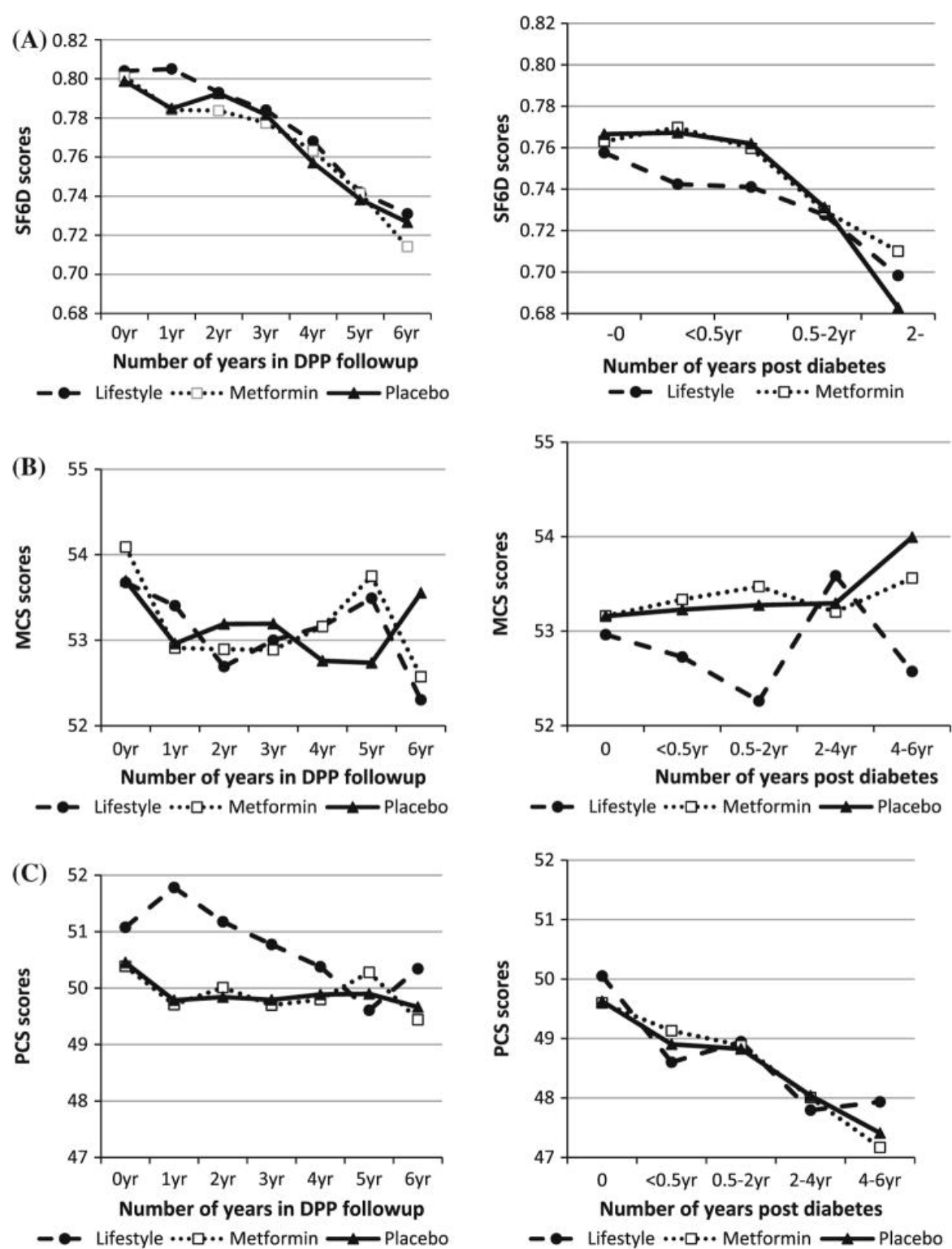
A recent review has brought together the different measures popularly used to assess quality of life and other outcomes in diabetes (33). These can be divided into measures that predominantly assess health status, those that predominantly assess diabetes specific quality of life, and those that assess generic quality of life. Table 1 summarises these measures.

1.2.4 What happens to quality of life in diabetes?

People with Type 2 diabetes report poorer quality of life than those without the disease. However, they do have better quality of life than people with most other chronic diseases.

Unlike Type 1 diabetes, there seems to be little impact of diagnosis of Type 2 diabetes on quality of life. Early studies suggested quality of life dipped initially at diagnosis but soon returned to normal levels (35–37). Since then, the best evidence of the change in quality of life that occurs following diagnosis comes from the American Diabetes Prevention Program (DPP) and its long term follow up study, the Diabetes Prevention Program Outcomes Study (DPPOS) (38). DPP was a landmark randomised control trial comparing the ability of an intensive lifestyle intervention (ILS), metformin treatment (MET) and placebo (PLB) to prevent the development of Type 2 diabetes in those with impaired glucose tolerance. Despite the interventions, some patients went on to develop Type 2 diabetes. This provided a unique opportunity to analyse changes in quality of life from around the time of diagnosis to up to 6 years after. Quality of life was assessed using the SF-36 questionnaire, a widely used measure of generic health-related quality of life. Subscale scores in different health domains were combined to produce two composite scores. The Physical Component Summary (PCS) and Mental Component Summary (MCS). Score across all domains were used to produce an overall score of health state called SF-6D. In all participants diagnosed with diabetes, PCS and SF-6D scores declined over the course of the trial. MCS scores were stable in all arms except for an initial fall in participants in the ILS arm but this difference did not persist. These results suggest there is a gradual decline in quality of life in the first years following a diagnosis of Type 2 diabetes. The fact it declined in all trial arms suggests this is part of the natural progression of the disease.

Figure 4 – Quality of life results from the DPPOS, split into SF-6D score of overall health, Mental Component Summary (MCS) of SF-36, and Physical Component Summary (PCS) of SF-36. Taken from Marrero et al. (38).



1.2.5 What is quality of life in diabetes associated with?

In long duration Type 2 diabetes, declining quality of life is seen with the development of both microvascular and macrovascular complications. The United Kingdom Prospective Diabetes Study (UKPDS) was a landmark study which aimed to answer the fundamental question of whether improved blood glucose control reduces the incidence of complications, and whether different treatments have specific advantages or disadvantages (39). Quality of life was measured in a cohort of over 5000 participants using the generic EuroQol - 5 Dimensions (EQ-5D) measure of health status. It found in the year following the development of a microvascular and macrovascular complication quality of life declined significantly. However, they saw no effect of different treatments on quality of life.

In addition a large scale survey of people with Type 2 diabetes in a primary care setting found the reduction in quality of life and was primarily related to the presence of microvascular complications, heart disease, depression and high number of diabetes medications (40). The survey took place in the US, reported on 909 individuals, and used a generic measure of health related quality of life called the Health Utility Index. There were also weaker associations between reduced quality of life and older age, female sex, lower education level and diabetes duration.

1.2.6 How do lifestyle interventions affect quality of life?

Effects in newly-diagnosed Type 2 diabetes

Participants receiving the intensive lifestyle intervention in the American DPP/DPPOS experienced a worse decline in quality of life than those in the metformin or placebo treated arms (Figure 4) (38). In addition, participants in the ILS arm experienced an immediate decline in MCS score following diagnosis but their trajectory returned to one similar to the metformin and placebo treated arms. This reduction may have been due to disappointment at having developed diabetes despite their efforts to prevent it. Interestingly, participants in the ILS arm who remained diabetes-free experienced an improvement in PCS score in the first year but then declined gradually over the trial, suggesting they were able to delay this decline.

However, results of the DESMOND study suggest behavioural lifestyle interventions can be delivered without reducing quality of life. The British Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND) study was multicentre cluster randomised control trial assessing the effects of a 6-hour comprehensive group-based lifestyle advice and education intervention in newly diagnosed Type 2 diabetes (41). Practices assigned to control were resourced to provide an enhanced usual care with contact time with healthcare staff equivalent to those in the intervention arm. Resources were used by practices as they saw fit within their usual care routine. Quality of life was assessed using the WHOQOL-BREF. There was no difference in subscale scores between the interventions and control arms after one year of follow up. There was also no difference between the groups in diabetes distress as assessed by the PAID questionnaire, and no difference in depression as assessed by the HADS. Illness perception was measured by the revised Illness Perception Questionnaire. Results showed those in the intervention group had a greater understanding of their illness and seriousness, a better perception of its duration, and a better understanding of their ability to influence the course of their illness. It is important to note the enhanced usual care delivered to the control arm may have contributed to the lack of difference between arms.

Effects in established Type 2 diabetes

The Action for Health in Diabetes (Look AHEAD) study showed those in the lifestyle intervention arm experienced a slower decline in quality of life (42). This was a landmark study in Type 2 diabetes that aimed to assess the long-term impact of a weight loss lifestyle intervention on cardiovascular morbidity and mortality. It included more than 5000 participants who were cluster randomised to the intensive lifestyle intervention (ILI) group or a diabetes support and education (DSE) control arm. The intensive lifestyle intervention targeted aggressive weight loss of 10% through dietary changes, exercise prescription and physical activity advice, as well as weight lowering medications such as Orlistat (43). Patient-reported outcome measures were recorded during the trial, including quality of life measured using the SF-36. There was a significant difference between the groups in the Physical Component Summary (PCS). Although scores in both groups declined during the trial, the rate of decline was

slower in the ILI group compared to the DSE group. There appeared to be no effect of the intervention on the Mental Component Summary (MCS), with scores remaining relatively stable in both groups throughout the trial. These results suggest an intensive lifestyle intervention may mitigate the decline in physical function seen with ageing.

Effects of physical activity and diet types

Evidence of the effect of different exercise types on quality of life, psychological wellbeing, depressive symptoms, and anxiety is limited and provides conflicting results (44). The most recent systematic review looking at the effects of exercise on quality of life and wellbeing reported in 2013. Of 20 RCTs included, 16 studies assessed quality of life. Of the 16 RCTs assessing quality of life; 6 assessed the effect of aerobic training, 4 the effect of resistance training and 10 the effect of combined training. Aerobic training improved physical health and sleep in one RCT but there was no change in quality of life in all the other studies. Resistance training showed highly conflicting results, with one short duration study showed improved quality of life in favour of the intervention group but another longer duration study showed a significant, albeit small, difference in favour of control. Combined training again returned mixed results with 3 studies showing training improved quality of life, 1 showing training reduced quality of life, and 6 showed no change in quality of life.

A direct comparison between supervised exercise and physical activity advice showed supervised exercise and physical activity advice resulted in improved quality of life compared to physical activity advice alone. The Italian Diabetes and Exercise Study (IDES) was a large randomised trial with glycaemic control as the primary outcome. Quality of life was measured using SF-36.

Improvements were seen in both PCS and MCS scores, with the greatest effect size seen in PCS. Particular improvements were seen in role limitations due to physical functioning, bodily pain, and general health perception. However, in this study the amount of contact time between each of the interventions was vastly different, being higher in the supervised arm, and this may explain the difference.

The effect of dietary changes alone on quality of life in people with Type 2 diabetes is a very under-researched area. This was highlighted in the 2007 Cochrane Review of the effect of diet in Type 2 diabetes. To date there has not

been a meta-analysis or systematic review assessing the impact of different dietary changes on quality of life in people with Type 2 diabetes. However, a recent systematic review and meta-analysis of the use of carbohydrate restriction in the management of Type 2 diabetes analysed quality of life changes in studies specifically comparing low carbohydrate diets (LCD) and high carbohydrate diets (HCD) (45). Quality of life was measured in just 5 of the 10 studies included in the meta-analysis. In the two studies that assessed generic HRQoL using the SF-36, there was no difference in MCS score, but overall PCS scores declined more in those receiving the LCD intervention compared to a HCD. In the three other studies that used other questionnaires, there was no difference in scores between arms, including one trial that used the disease-specific Diabetes-39 (D-39) tool.

In the context of obesity, a systematic review of weight loss through dietary changes has reported quality of life is improved by weight loss, but significant levels of weight loss are required. At the time of the review, evidence at randomised control trial level was lacking. However since then the Diabetes Remission Clinical Trial (DiRECT) has reported (22). The DiRECT study assessed the ability of a primary care-led low-calorie diet intervention to achieve remission of Type 2 diabetes in overweight people. It is the first and only randomised control trial of a dietary intervention with the primary outcome of remission of diabetes. Remission was defined as a sustained return of HbA1c to non-diabetic levels ($<48\text{mmol/mol}$), after at least two months without diabetes medication. The intervention involved a weight loss induction phase using a low-calorie formula diet for 3-5 months, followed by structured re-introduction of food over the 2-8 weeks, with subsequent ongoing weight management. Diabetes and antihypertensive medications were stopped on day 1 of the intervention. This intervention resulted in diabetes remission in 46% of participants. Remission was also heavily associated with weight loss across the whole study. 86% of people who achieved weight loss of $\geq 15\text{kg}$ achieved remission and just 7% of those who lost 0-5kg. As well as achieving a higher rate of remission, individuals in the intervention arm experienced an improvement in quality of life as measured by EQ-5D VAS of 6.4 points (95% CI 2.5, 10.3; $p=0.0012$).

1.2.7 How was it measured in this project?

In this study quality of life was measured using the EuroQoL- 5 Dimensions (EQ-5D) (see Appendix 1). The EQ-5D is a widely used measure of preference based health-related quality of life. It has been used in populations across the world, across a number of different diseases. The EQ-5D is composed of two parts. Part one is a questionnaire with 5 items (dimensions): Mobility, Self-Care, Usual activities, Pain/discomfort, and Anxiety/depression. Each dimension is answered on a 3 level scale. 1 represents no difficulty, 2 represents some difficulty, 3 represents severe difficulty (e.g. unable to mobilise). The resulting set of responses is converted to an index score of overall health by an algorithm using population-specific coefficients. Part two of the questionnaire is a Visual Analogue Scale (VAS) where participants are asked place a point on a line of 0-100 where they think they are on the line, with 0 representing the worst imaginable health state and 100 representing the best imaginable health state.

The use of the EQ-5D in adults with Type 2 diabetes has recently been reviewed (46). This identified 54 relevant publications and aimed to summarise the validity, reliability and responsiveness of the EQ-5D in diabetes, and provide a catalogue of scores of various subgroups and complications. It found the spread of values of health index value in keeping with what was expected, with end-stage renal failure and severe diabetic neuropathy pain at the lower end of health index and comorbidities such as treated hypertension at the higher end. Overall, it found the EQ-5D displayed construct, convergent and discriminant validity. Reliability ranged from good to excellent and it was similarly responsive as other measures like the SF-12 and SF-36. However, several studies noted a ceiling effect. This is a well-known limitation of the EQ-5D and led to the development of a 5-level version.

1.3 Wellbeing

1.3.1 What is wellbeing?

Wellbeing is different to quality of life in that it focuses on mental health and by extension mental illness. This includes constructs such as affect, self-esteem and subjective wellbeing, as well depression and anxiety (47).

1.3.2 How is it measured in diabetes?

Similar to quality of life, wellbeing is commonly assessed using multiple-item questionnaires. These measures are required to both valid and reliable and can be divided into those that measure general wellbeing and those that measure diabetes specific wellbeing. The most commonly used measures in diabetes are given in Table 1.

1.3.3 How does Type 2 diabetes affect wellbeing?

Type 2 diabetes is associated with a variety of psychological problems. The two major associated psychological conditions are depression and psychological distress.

Type 2 diabetes and depression are heavily associated. People with type 2 diabetes are 24% more at risk of developing depression than non-diabetic individuals (48). The prevalence of depression with Type 2 diabetes is almost double that of people without diabetes (18% vs 10%) (49). In addition, comorbidity with depression seems to be related to the burden of a diagnosis of chronic disease, with significantly lower risk of depression in patients with impaired glucose metabolism or undiagnosed diabetes compared to those with a diagnosis of Type 2 diabetes (50).

Type 2 diabetes also often results in significant emotional distress. A recent systematic review has reported on disease specific “diabetes distress” (51). Diabetes distress describes the broad array of distinct emotional concerns surrounding the experience of living with diabetes, a chronic and progressive disease. This can include feeling overwhelmed by the responsibility of managing their own condition through self-monitoring and lifestyle changes, as well as worry over possible future progression to insulin and/or development of complications. They may also fear hypoglycaemia or suffer feeling of guilt or shame relating to obesity and/or lifestyle choices (51,52). The findings of the

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systematic review were that diabetes distress was a significant issue estimated to affect 36-46% of people with Type 2 diabetes. It is more common in women than men and more common in those with depressive symptoms.

1.3.4 What effects does wellbeing have on Type 2 diabetes?

Diabetes and depression is thought to be a bi-directional relationship, with those suffering depressive symptoms more likely to experience self-neglect, and perhaps more likely to have unhealthy lifestyles predisposing them to the development of Type 2 diabetes (53). Depression was also associated with poorer glycaemic control in a meta-analysis albeit with a small effect size (54).

There is also evidence of poor diet and exercise habits in people with Type 2 diabetes and persistent or worsening depressive symptoms (55). In addition, Sumlin et al. performed a systematic review of the association between depression and adherence to diet and physical activity lifestyle changes (56). They pooled data from 7266 participants. Twenty-one descriptive studies were identified and showed a negative relationship between depression and adherence to diet and physical activity lifestyle changes. Only two of six interventional studies assessed this relationship and had conflicting evidence. The reviewers noted there was likely a true association however RCT-level evidence is both limited and conflicting.

Diabetes distress, like depression, is associated with poorer glycaemic control. Both could be explained by a direct effect through dysregulation of stress hormones, or by depressive symptoms and distress both leading to poor self-care (52,57).

1.3.5 How does treatment affect wellbeing in Type 2 diabetes?

A 2013 systematic review of exercise on quality of life and wellbeing found four studies that examined the effect on depression (44). Results were inconclusive. Two short duration studies of aerobic exercise found no difference in depressive symptoms between intervention and control. A further study of home-based combined aerobic and resistance training interventions again found no difference in depressive symptoms. However, these studies were all limited by short duration (less than 8 weeks). There was however one longer duration

study (16 weeks) which showed resistance exercise reduced depressive symptoms.

The same review identified the effect of aerobic training on other aspects of wellbeing including anxiety (44). Wellbeing in all studies was assessed using the W-BQ 12 or its parent questionnaire the W-BQ 22. There was conflicting evidence as some shorter duration studies of aerobic and resistance exercise found improvements in wellbeing and reduced anxiety. However, a longer duration study found no difference between intervention and control after aerobic, resistance and combined aerobic and resistance exercise (58).

Since this review, the landmark Look AHEAD trial has reported its wellbeing results. It assessed depressive symptoms using the Beck Depression Inventory over 8 years of follow up and found the intensive lifestyle intervention (ILI) reduced the risk of developing depression by 15% compared with control (DSE) (42).

1.3.6 How was it measured in this project?

Wellbeing was assessed in two domains; self-esteem and life satisfaction.

Life satisfaction

Life satisfaction was assessed using Diener's Satisfaction with Life Scale (SWLS). It is a measure developed to assess global satisfaction with life, a key component of subjective wellbeing. Subjective well-being is composed of three separate components, positive affect, negative affect and life satisfaction. Whilst the first two components refer to the emotional side of subjective wellbeing, overall life satisfaction is a much more cognitive process. Life satisfaction is defined as a "global assessment of a person's quality of life according to his/her chosen criteria" (59).

The scale is composed of 5 items on a 7 point Likert scale from Strongly Agree to Strongly Disagree. The 5 items are:

- In most ways my life is close to ideal
- The conditions of my life are excellent
- I am satisfied with my life
- So far I have gotten the important things I want in life
- If I could live my life over, I would change almost nothing.

The five items are all positive worded so a sum score of life satisfaction can be produced by adding scores together.

A 1985 review of questionnaires assessing subjective wellbeing found the SWLS compared favourably with other instruments (60). It had excellent test-retest reliability, high internal consistency despite being only 5 items, and converged well with other measures. However, a vulnerability to social desirability bias was highlighted.

Overall, it is one of the most popular scales used to measure life satisfaction. It has been validated in a huge variety of populations, including those with diabetes.

Self-Esteem

Self-esteem was measured using the Rosenberg Scale of Self-esteem (RSES). It is one of the most widely used instruments in the history of psychology. Originally designed for adolescents it has been validated and used extensively across adults of all ages. The scale is composed of 10 items; 5 positive statements and 5 negative statements. Originally designed as Guttman Scale with complex scoring, many have since used a sum score, reversing the negatively worded items. This approach has been adopted by most people since (61,62).

The 10 items of the scale are:

- I feel that I am a person of worth, at least on an equal plane with others.
- I feel that I have a number of good qualities
- All in all, I am inclined to think I am a failure.
- I am able to do things as well as most other people.
- I feel I do not have much to be proud of.
- I take a positive attitude toward myself.
- On the whole, I am satisfied with myself.
- I wish I could have more respect for myself.
- I certainly feel useless at times.
- At times I think I am no good at all.

Each item is rated from Strongly Agree to Strongly Disagree on a 4-point scale.

The scale has excellent test-retest reliability and internal consistency. It demonstrates concurrent, predictive and construct validity. It correlates well with other measures and has negative associations with expects factors such as anxiety and depression (62).

1.4 Treatment Satisfaction

1.4.1 What is treatment satisfaction?

Treatment satisfaction is a global assessment of an individual's experience of their treatment across all aspects. As treatments are very specific to a disease, disease specific measures are generally favoured.

1.4.2 How is it measured in diabetes?

Much like with quality of life and wellbeing treatment satisfaction is normally assessed using validated questionnaires. The most widely used is measure is the almost universally adopted Diabetes Treatment Satisfaction Questionnaire (DTSQ) (Table 1) (63). It is the treatment satisfaction tool recommended by the World Health Organisation (WHO) and International Diabetes Federation (IDF) (64).

1.4.3 How does treatment satisfaction vary across different diabetes treatments?

The reason treatment satisfaction is very important in diabetes is treatments are often judged almost entirely on their ability to reduce HbA1c. However, treatments can have the same HbA1c response but can be hugely different experiences for people receiving the treatment. For this reason treatment satisfaction in diabetes has recently been reviewed (65).

An example of this scenario is in rapid-acting insulin analogues. Whilst they result in a similar change in HbA1c as treatment with human insulin, the increased flexibility and reduced risk of hypoglycaemia results in far greater treatment satisfaction (66). Similar improvements in treatment satisfaction despite no difference in HbA1c have been seen in studies comparing long-acting insulins to neutral protamine Hagedorn (NPH) insulin. This phenomenon is not restricted to insulin analogues, and has been seen in oral medications including incretin-related agents, SGLT-2 inhibitors, once weekly DPP-4 inhibitors and fixed dose combination tablets.

Lifestyle interventions have also been shown to improve treatment satisfaction. The Diabetes X-PERT study assessed the impact a lifestyle and self-management intervention in those with established Type 2 diabetes. Those in the intervention arm experienced improved treatment satisfaction compared to control (67).

1.4.4 Which factors are associated with changes in treatment satisfaction?

The authors of the review described above have attempted to answer this very question (65,68). Their study in a Japanese secondary-care setting found a number of factors associated with treatment satisfaction. They found improved satisfaction was associated with lower treatment intensity, with those treated through lifestyle changes alone experiencing the highest satisfaction and those on insulin treatment experiencing the lowest satisfaction. This was an expected finding although there is evidence of improved satisfaction with insulin treatment in poorly controlled diabetes (69).

Importantly they found treatment satisfaction was not related entirely to the intervention prescribed and care delivery was understandably very important. Treatment satisfaction was strongly associated with dissatisfaction with waiting times, satisfaction with consultation time, satisfaction with the attending doctor and satisfaction with the overall hospital visit. Satisfaction with the attending doctor was the most strongly associated factor highlighted that the treatment itself it not always the most important in determining satisfaction.

Interestingly, satisfaction with diabetes treatment was also associated with improved adherence and reduced dropout from treatment. The association with improved adherence was seen with diabetes medication and diet and physical activity therapies.

HbA1c was not associated with treatment satisfaction, a finding in keeping with some other studies (66). However, a large Dutch cohort study assessing quality of life and treatment satisfaction in people living with Type 2 diabetes revealed people with higher HbA1c levels, younger people, and people on insulin therapy were less satisfied with their treatment. There were also modest but statistically significant associations with EQ-5D Index and EQ-5D VAS (70).

1.4.5 How was it measured in this project?

The Diabetes Treatment Satisfaction Questionnaire (DTSQ) is a disease-specific measure of satisfaction with treatment developed in 1988 that has become widely used in diabetes research across the world (63). It is composed of 8 items. 6 items of the scale assess subjects' satisfaction with treatment across six areas; satisfaction, convenience, flexibility, understanding, likelihood to recommend, likelihood to continue. The other two items relate to how often subjects experience hypoglycaemia or hyperglycaemia.

The DTSQ demonstrates internal consistency, test-retest reliability, as well as content, convergent and concurrent validity. Although responsive to change, many have identified a ceiling effect and this led to the development of the DTSQ Change Version (DTSQc) to be used in tandem with the DTSQ with repeated-measure study designs (71).

1.5 Summary

1.5.1 *What we know*

Type 2 diabetes is a common chronic illness that can be successfully treated with lifestyle changes. Quality of life and wellbeing are affected by Type 2 diabetes and as such they are important treatment outcomes. Type 2 diabetes results in a reduction of quality of life, this decline being associated with the development of complications, associated depression, or the requirement of large numbers of medications. Despite improving a multitude of clinical outcomes, adherence to lifestyle interventions is poor. 40-51% of people with Type 2 diabetes are non-adherent. In addition, recent surveys have identified a number of barriers to dieting and exercising encountered by people with Type 2 diabetes, particularly those who are obese. These include the burden of dieting on quality of life, as well as physical discomfort, sweating or shame/stigma experienced when exercising.

1.5.2 *What remains unclear*

Trials of lifestyle interventions have provided conflicting results of their effects on quality of life, particularly early on the disease when they are most likely to be offered. The limited evidence suggests a modest decline in quality of life, particularly physical quality of life. However, other studies have shown no change in quality of life. Moreover, in some studies of people with established diabetes have shown improved quality of life and wellbeing as a result of lifestyle changes. Therefore, the effects of these interventions on wellbeing and quality of life need clarification.

Secondly, comorbid depression is associated with poor adherence to lifestyle interventions but the degree to which individuals' wellbeing and quality of life contribute to the poor adherence seen remains unclear.

Thirdly, what happens to quality of life and wellbeing over the first years following diagnosis of Type 2 diabetes prior to the development of complications is unclear. Evidence of the changes in quality of life that occur in this time is limited to one study and little is known about wellbeing over this period.

1.5.3 What this project aimed to add

This project used existing patient reported outcome measure data from the Early ACTivity In Diabetes (Early ACTID) randomised control trial (72). The trial compared dietary advice, diet plus physical activity advice and usual care in order to determine whether the addition of physical activity advice to dietary advice warrants the additional training of staff it would require. The main findings were firstly that dietary and physical activity interventions close to diagnosis improved HbA1c, use of diabetes medication, weight, waist circumference, and insulin resistance compared to usual care. Secondly, the addition of physical activity advice to dietary advice did not confer any additional benefit and so extensive retraining that would be required to deliver this intervention on a large scale is not justified.

I will use patient-reported outcome measure data from Early ACTID to answer three broad research questions of:

1. How do treatment satisfaction, quality of life and wellbeing change during the first 6 years following diagnosis of Type 2 diabetes?
2. What is the effect of lifestyle interventions on treatment satisfaction, quality of life and wellbeing in newly diagnosed Type 2 diabetes?
3. Are treatment satisfaction, quality of life and wellbeing associated with response to lifestyle interventions in Type 2 diabetes?

The project hypotheses were:

1. There is a modest decline in quality of life over time in all trial arms.
2. Treatment satisfaction is higher in the intervention groups compared to control.
3. Self-esteem and life satisfaction are improved by lifestyle interventions
4. Higher baseline self-esteem and/or life satisfaction is associated with greater improvements in HbA1c and weight loss.

Chapter 2 – Methods

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This project was made possible by existing data from a randomised control trial of lifestyle interventions. The trial was designed and carried out by principal investigator Prof R.C. Andrews, and the rest of the Early ACTID group.

2.1 The Early ACTID Trial

This thesis used existing patient-reported outcome measures data from the Early ACTivity In Diabetes (Early ACTID) randomised control trial. This Chapter will first describe the reasons behind the trial, and explain in full how it was performed using the CONSORT guidance as a reference. It will then provide a summary of the main findings of the trial and a spotlight on the patient-reported outcome measures used in the trial; how they are scored, and what the scores indicate,

The aim of the Early ACTID trial was to determine whether providing physical activity alongside dietary advice offered additional benefits above those seen when dietary advice is given alone in newly diagnosed Type 2 diabetes. At the time of the trial, people with new type 2 diabetes were offered one-to-one dietary advice, attendance at an education day, or both. The physical activity advice given in these interventions was usually very general as few healthcare workers are trained in this field. In order to justify additional training of large numbers of staff, a clear additional benefit of physical activity advice would need to be shown (72).

2.1.1 Trial Design

The Early ACTID trial was a multicentre, parallel group randomised control trial of lifestyle interventions in newly diagnosed Type 2 Diabetes. It had three arms; usual care, an intensive dietary intervention, and an intensive diet plus physical activity intervention.

2.1.2 Participants

Inclusion Criteria

1. Type 2 Diabetes as defined by
 - a. BMI greater than 25
 - b. No ketosis
 - c. No significant weight loss prior to diagnosis
2. Between 5-8 months from clinical diagnosis of Type 2 diabetes

Exclusion Criteria

1. Age over than 80 at diagnosis
2. HbA1c greater than 10%

3. Blood pressure greater 180/100mmHg
4. LDL greater than 4 units
5. Weight greater than 180kg
6. Individual already receiving a maximum dose of sulphonylurea
7. Current diagnosis of Unstable Angina
8. Myocardial Infarction within last 3 months
9. Unable to increase physical activity level
10. Individual pregnant or is of childbearing age and not surgically sterile or not using a form of contraception.

Withdrawal Criteria

1. The individual becomes pregnant, as evident by a positive pregnancy test
2. The investigator feels it is in the subject's best interest to be withdrawn

Setting

Participants were recruited through primary care and direct advertising via four recruitment centres.

- Taunton and Somerset NHS Trust, covering Somerset
- United Bristol Healthcare NHS Trust, covering North Somerset
- North Bristol NHS Trust, covering North Somerset
- Gloucestershire Hospitals NHS Trust, covering Gloucestershire

Location

The trial took place across 7 sites in South West England.

- Taunton and Somerset NHS Trust Musgrove Park Hospital
- Weston General Hospital
- Cheltenham General Hospital
- Gloucestershire Royal Hospital
- United Bristol Healthcare
- Frenchay Hospital
- Southmead Hospital

2.1.3 Interventions

Timeline of Visits

The timeline of visits and differences between numbers of visits by participants in each arm during the Early ACTID trial is given in Table 1.

Table 1 – *Timeline of visits in Early ACTID*

Time (wks)	Visit	Action	Standard care	Diet alone	Diet plus activity
-6	1	Consent and screening	✓	✓	✓
-4	2	Fitness test	✓	✓	✓
-2	3	Consent qualitative study and baseline measurements	✓	✓	✓
		Randomisation data is collated & prepared prior to visit 4			
0	4	Clinical review & randomisation to treatment arm	✓	✓	✓
2	5	Nurse visit		✓	✓
4	6	Nurse visit		✓	✓
6	7	Nurse visit		✓	✓
10	8	Nurse visit		✓	✓
14	9	Nurse and Dietitian visit		✓	✓
20	10	Nurse visit		✓	✓
26	11	6 month measurements	✓	✓	✓
28	12	6 month fitness test	✓	✓	✓
32	13	Doctors and dietitian (nurse for standard care arm) review visit	✓	✓	✓
38	14	Nurse visit		✓	✓
42	15	Nurse and dietitian visit		✓	✓
46	16	Nurse visit		✓	✓
52	17	12 month measurements	✓	✓	✓
54	18	12 month fitness test	✓	✓	✓
58	19	Doctor and dietitian review – discharge plan	✓	✓	✓

Usual Care

Participants in the usual care arm received doctor, dietary and nursing advice at baseline. They were then seen at 6 and 12 months by both a doctor and nurse.

In the dietary session, dietitians gave standard advice about diet and provided the patients with a patient information sheet detailing the recommended diet for those in the two intervention arms. Nurses provided general advice about exercise and monitoring of urine (or blood where applicable). Participants were also given the contact details of the Early ACTID team and were able to organise sessions with a nurse if they had problems regarding the management of their disease.

Intensive Dietary Intervention

Participants in the intensive dietary intervention received usual care as well as a comprehensive dietary intervention with nine additional sessions with a nurse or dietitian over the 12 months (Table 1).

The primary goal of the intervention was for participants to achieve a weight loss of 10% of their initial body weight and maintain that weight loss throughout the trial. The recommended pace of this weight loss was 0.5-1kg per week to produce 5% weight loss in approximately 12 weeks.

This weight loss would be achieved by the establishment of a hypo-energetic diet, based on an energy deficit of approximately 500kcal within the context of general guidelines for a healthy diet.

Sessions included advice on

- Healthy eating
- Meal frequency
- Sugar
- Special diabetic foods
- Alternative sweeteners
- Fats
- Carbohydrates
- Fibre
- Alcohol
- Salt

- Management of illness
- Understanding food and nutrition levels
- Eating out
- Shopping tips

Sessions were based around the setting of personalised goals. Participants recorded a food diary for 4 days prior to each session. Using this participant and dietitian discussed potential changes and came up with agreed personal targets.

Individuals who wanted to achieve greater than 10% weight loss were encouraged to do so provided their resultant BMI would be greater than 24. In addition, weight loss of greater than 2kg per week was not advised due to safety. Individuals who struggled to meet the weight loss target set personalised goals that were more achievable, but it was important they remained challenging.

A key aim of the intervention was to not only achieve weight loss, but to maintain it over the longer term. Therefore, the sessions aimed to provide with the necessary skills and behaviours to main their weight successfully over in the long term.

Intensive Dietary and Physical Activity Intervention

Participants in the diet and physical activity arm received all components of the usual care and intensive dietary intervention, as well as a physical activity advice intervention

The physical activity intervention aimed to achieve and maintain a 700kcal additional energy expenditure per week through moderate-to-vigorous physical activity (equivalent to 150 minutes walking). It was described to participants as half an hour of brisk walking at least 5 days each week for ease of understanding. This goal was applied to all participants, independent of their existing physical activity level.

The physical activity level was increased step-by-step over 5 weeks. During the first week participants were encouraged to do something active 3 to 4 days per week. In the subsequent weeks the activity level was increased to 60, 90, 120 and finally 150 minutes per week. The physical activity target was a minimum

target. Participants who wished to do more exercise were encouraged to do so. Participants who were already active had to add a further 150 minutes of activity to meet their goal. In addition, those who were seasonally active were encouraged to spread their physical activity consistently over the months of the trial.

Participants measured their activity levels using hip worn activity monitors and recording an activity log. Participants were requested to keep their activity log daily and record the time of day and reading when the device was put on and then when it was taken off at the end of the day. They were also requested to record the reading before and after walking periods and the duration of the activity. Data was used to monitor physical activity levels achieved and to identify the presence or absence of any compensatory sedentary behaviour.

A key strategy of the intervention was to empower participants with the confidence to exercise. This was achieved by practitioner and participant setting negotiated, realistic and achievable targets. This was supported by participants self-monitoring of their progress towards the target.

Adjustments to the intervention were made where participants did not wish to choose walking as their activity. The options to choose alternative exercise forms was open and those who wished to do more vigorous exercise such as running, had the duration of their activity tailored towards achieving the 700kcal weekly energy expenditure target. For those participants who found the physical activity targets difficult, personalised goals were made, as well as the provision of input from a fitness trainer and/or discounted gym memberships.

Control of other factors

To attempt to negate the potential impact of increased contact time, the study was designed to ensure participants in both intervention arms received the same amount of contact time. In both intervention arms, one half of each session was allocated to discussion of dietary changes. In the dietary intervention arm, the other half of the session was dedicated to patient-led discussion of lifestyle topics of their choice. In contrast, for those in the dietary and physical activity intervention arm the other half was dedicated to the physical activity advice.

To attempt to negate the potential impact of medication changes, steps were made to limit changes that occurred. During the study the trial team took over the care of all participants and any changes to medication were made according to a standardised protocol. In addition all doctors making the changes were blinded to arm allocation. Figures 1-4 display this protocol in full. In addition to this, ethical approval was given for no changes to diabetes and blood pressure medications to be made during the first 6 months to enable evaluation of the true effect of the interventions.

Figure 1 - Diabetes Medication Protocol for first 6 months of Early ACTID

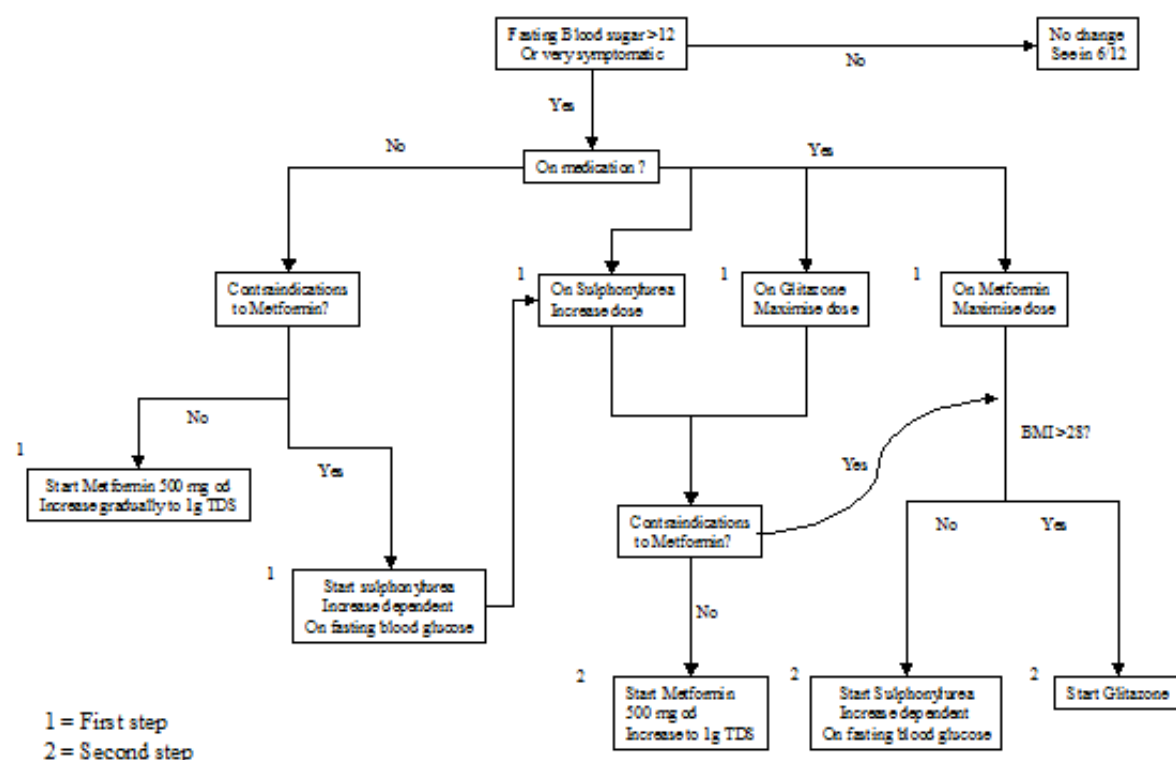


Figure 2 - Diabetes Medication Protocol for second 6 months of Early ACTID

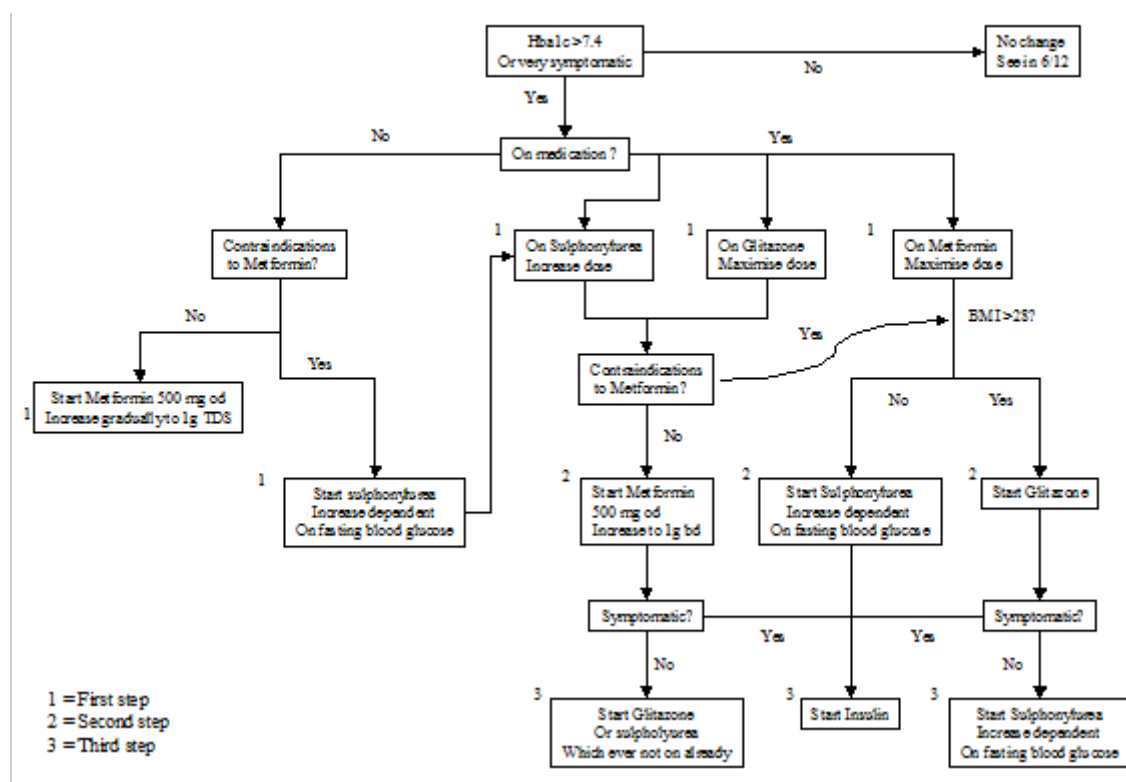


Figure 3 – Blood pressure medication protocol for first 6 months of Early ACTID

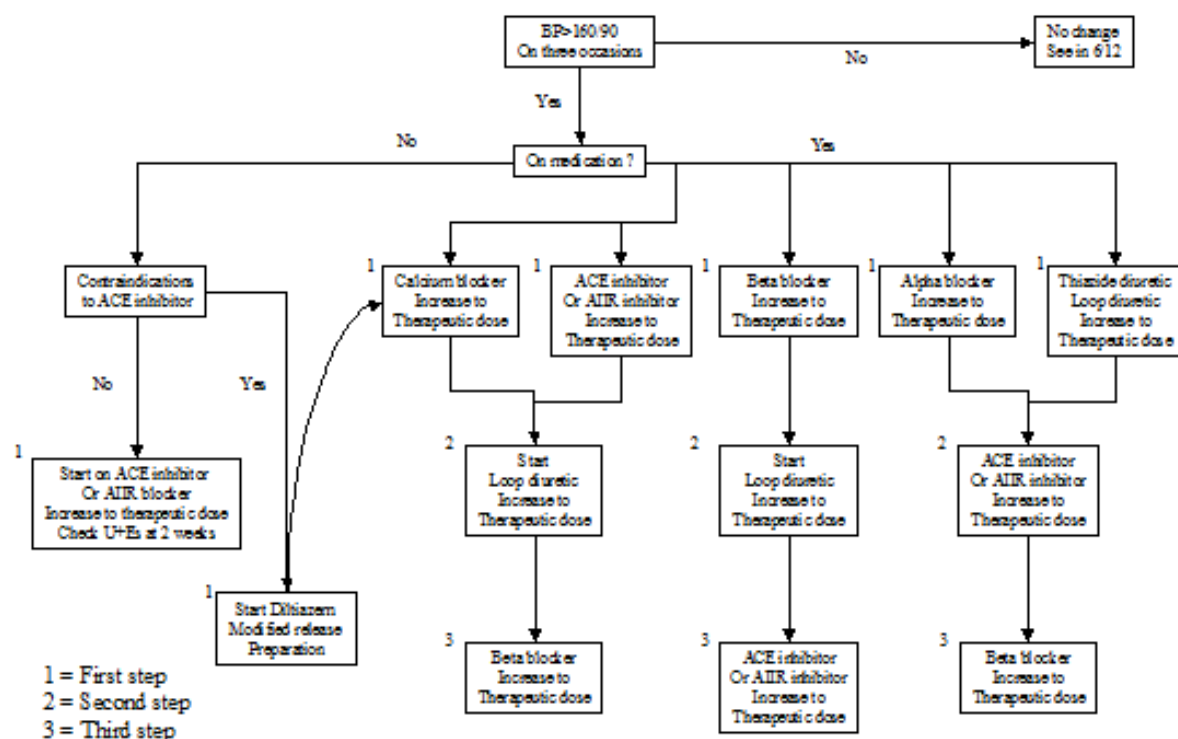
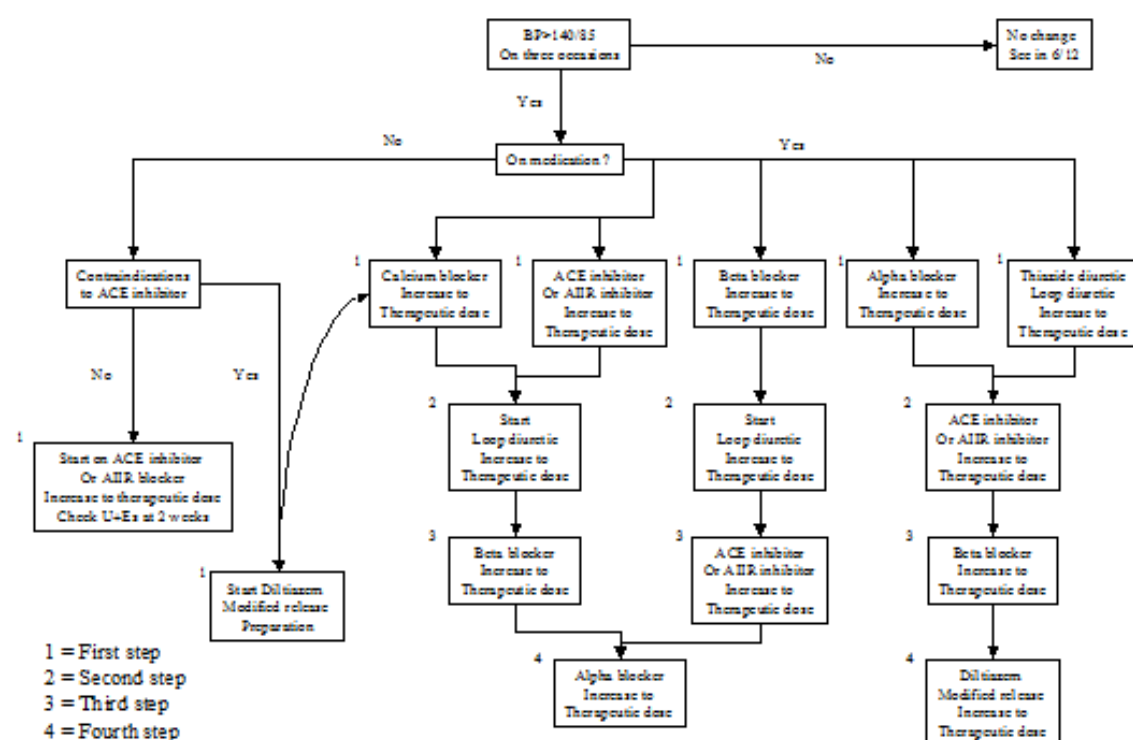


Figure 4 – Blood pressure medication protocol for second 6 months of Early ACTID



2.1.4 Outcomes

Primary Outcomes

- Glycaemic Control as measured by HbA1c at 6 months
- Systolic and diastolic blood pressure at 6 months

Secondary Outcomes

- Glycaemic control as measured by HbA1c at 12 months
- Systolic and diastolic blood pressure at 12 months
- Fasting lipid profile (Total cholesterol, HDL, LDL and TG)
- Insulin resistance (measured by HOMA)
- Insulin secretion (measured by HOMA)
- Weight (kg)
- BMI
- Body composition
- Waist and hip circumference
- Cardiovascular fitness (measured by mile walk test)
- Amount of diabetes, blood pressure and Lipid medication required
- Activity measured by Actigraph at baseline, 6 and 12 months
- Questionnaires
 - Physical Activity
 - PARQ
 - Stage of change towards exercise
 - Self-efficacy towards exercise
 - Process of change
 - Social support for physical activity scale
 - Decisional balance
 - Outcome expectations for exercise
 - Sleep
 - Epworth Sleepiness Scale
 - The Sleep Habit questionnaire
 - Wellbeing
 - Satisfaction with Life Scale (SWLS)
 - Rosenberg Self-Esteem Scale
 - Euroqol – 5 Dimensions (EQ-5D)

- Diabetes Treatment Satisfaction Questionnaire (DTSQ)
- Brief Illness Perception Questionnaire (BIPQ)
- Diaries
 - 1 week sleep diary
 - 4 day food diary

2.1.5 Sample size

Originally the planned sample size was 750 participants, allocated in a 1:1:1 ratio to diet, diet and physical activity and usual care. With HbA1c and blood pressure the primary outcomes, this sample size was determined in order to be able to detect between group differences in these parameters. The standard deviation of HbA1c among people with diabetes is reported at 1.87% and the minimum clinically important difference is reported at 0.5%. This is equivalent to an effect size of 0.27 SD. For blood pressure this equates to 4.5mmHg in systolic and 2.3mmHg in diastolic blood pressure. Due to high retention and slower than expected recruitment, this was amended to 546 participants split in a 5:5:2 ratio (216 in each intervention arm and 86 in the control arm). The original sample size provided 90% power, but the revised minimum target of 546 participants split in a 5:5:2 ratio provided 80% power with a 5% two-sided alpha to detect differences of 0.27 SD between intervention arms, and power to detect a difference of 0.4 SD between an intervention arm and usual care. This allowed for 5% of data missing. 593 participants ended up being recruited. 99 were assigned usual care, 248 the diet intervention, and 246 the diet and activity intervention. It was decided it would have been unfair not to randomise people who had been consented after the target sample size of 546 had been reached.

2.1.6 Randomisation

Randomisation was performed by computer generated allocation. Participants were assigned in a 2:5:5 ratio to intensive dietary intervention, intensive dietary and physical activity intervention and usual care. Allocations remained concealed until participants attended visit 4 when they saw a dietitian who phoned the trial coordinator to retrieve the allocation code. Allocation was stratified by centre and minimised by age, sex, fitness, route into study and blood pressure..

2.1.7 Blinding

The nature of the intervention meant nurses, dietitians and participants were unable to be blinded. Doctors were blinded. Assessments were done by nurses.

2.1.8 Statistical Methods

As per CONSORT guidance the primary outcomes were reported using an intention-to-treat analysis.

In this project questionnaire data was analysed in two ways.

- To assess the between arm differences during the trial, T-tests of change from baseline score were used. Significance was achieved at $p < 0.0167$ after Bonferroni correction. Participants were included in this analysis if they completed all items of at least one questionnaire at baseline and after 12 months. This is described in full in the methods section of Chapter 3.

Analysis of the trends in quality of life during long-term follow up treated the participants as a single cohort and assessed longitudinal changes using multilevel mixed effects linear regression. This is described in full in the methods section of Chapter 4.

2.2 ACTID Plus

ACTID Plus was the long-term follow up study of Early ACTID participants. Following completion of Early ACTID, participants were contacted and re-consented to enter ACTID Plus. ACTID Plus followed up participants with annual visits for 5 years following completion of the program (6 years post-randomisation). This is shown in Table 2.

Table 2 – *Timeline of visits in ACTID Plus*

Follow-up phase					
104	20	Re-consent, 2 year measurements	✓	✓	✓
156	21	3 year measurements	✓	✓	✓
208	22	4 year measurements	✓	✓	✓
260	23	5 year measurements	✓	✓	✓
310	24	6 year measurements	✓	✓	✓

Where participants did not wish to attend in person some agreed to share their GP records and be followed up annually through primary care. The same measurements were recorded at each follow up point as in Early ACTID.

There were three major aims of the ACTID Plus study.

- The first aim was assess whether diet and diet plus activity intervention had lasting beneficial effects compared to usual care in terms of weight, glycaemia, blood pressure, lipid profile, insulin resistance, and medication requirement.
- The second aim of ACTID Plus was to assess whether these interventions had lasting beneficial effects compared to usual care in terms of eating patterns, physical activity habits, and patient-reported outcome measures.
- The third and final main aim of ACTID Plus was to determine whether these effects, if seen, are greater in the diet and physical activity arm than in the diet only arm of the trial.

2.3 Wellbeing Measures in Early ACTID and ACTID Plus

At each measurement visit of Early ACTID and ACTID Plus, participants were asked to complete paper copies of 5 patient-reported outcome measures that assessed the impact of diabetes on their wellbeing. The exact document provided to participants at each visit is given as Appendix 1. This section outlines the scoring of each of the measures used in Early ACTID and ACTID Plus.

2.3.1 Diabetes Treatment Satisfaction Questionnaire (DTSQ)

The Diabetes Treatment Satisfaction Questionnaire (DTSQ) is a disease-specific measure of satisfaction with treatment. It is composed of 8 items. 6 items of the scale assess subjects satisfaction with treatment across six areas; satisfaction, convenience, flexibility, understanding, likelihood to recommend, likelihood to continue. The other two items relate to how often subjects experience hypoglycaemia or hyperglycaemia. Each item is answered on a 7-point Likert scale (0-6). A sum score of overall satisfaction is calculated by adding together the scores of the six satisfaction items (73).

2.3.2 EuroQol – 5 Dimensions (EQ-5D)

The EQ-5D is a widely used measure of preference based health-related quality of life. The EQ-5D is composed of two parts.

Part one is a questionnaire with 5 items (dimensions): Mobility, Self-Care, Usual activities, Pain/discomfort, and Anxiety/depression. Each dimension is answered on a 3 level scale. 1 represents no difficulty, 2 represents some difficulty, 3 represents severe difficulty (e.g. unable to mobilise). The resulting set of responses is converted to an index score of overall health by an algorithm using population-specific coefficients.

Part two of the questionnaire is a Visual Analogue Scale (VAS) where participants are asked place a point on a line of 0-100 where they think they are on the line, with 0 representing the worst imaginable health state and 100 representing the best imaginable health state (46).

2.3.3 Brief Illness Perception Questionnaire (BIPQ)

The Brief Illness Perception Questionnaire (BIPQ) was developed as a shortened version of the Illness Perception Questionnaire (IPQ). Composed of 9 items, it aims to assess a number of cognitive and emotional representations of illness. Eight items assess perceived illness threat across eight areas related to their illness: consequences, timeline, personal control, treatment control, identity, concern, understanding and emotional response. The final item is a free-text item where subjects report their perceived illness cause.

The 9 questions are:

- How much does your illness affect your life?
- How long do you think your illness will continue?
- How much control do you feel you have over your illness?
- How much do you think your treatment can help your illness?
- How much do you experience symptoms from your illness?
- How concerned are you about your illness?
- How well do you feel you understand your illness?
- How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed)
- Please list in rank-order the three most important factors that you believe caused your illness. The most important causes for me:-

The first 8 items of the BIPQ can be used to create an overall sum score of perceived illness threat by reversing the negatively worded items (74,75).

2.3.4 Satisfaction with Life Scale (SWLS)

Diener's Satisfaction with Life Scale (SWLS) is a measure developed to assess global satisfaction with life. Life satisfaction is defined as a "global assessment of a person's quality of life according to his/her chosen criteria".

The scale is composed of 5 items on a 7 point Likert scale from Strongly Agree to Strongly Disagree. The 5 items are:

- In most ways my life is close to ideal
- The conditions of my life are excellent
- I am satisfied with my life

- So far I have gotten the important things I want in life
- If I could live my life over, I would change almost nothing.

The five items are all positive worded so a sum score of life satisfaction can be produced by adding scores together. The possible range of scores is therefore 5 to 35, with 20 representing the scales neutral point (60,76).

Sum scores can be interpreted as:

- 5 to 9 – Extremely dissatisfied with life
- 15 to 19 – Slightly dissatisfied with life
- 20 to 24 – Neutral point
- 21 to 25 – Slightly satisfied with life
- 31 to 35 – Extremely satisfied with life

2.3.5 Rosenberg Self-Esteem Scale (RSES)

The Rosenberg Self-Esteem Scale is composed of 10 items; 5 positive statements and 5 negative statements. Originally designed as a Guttman Scale with complex scoring, we instead used a sum score, reversing the negatively worded items. This is a commonly used approach to scoring (62).

The 10 items of the scale are:

- I feel that I am a person of worth, at least on an equal plane with others.
- I feel that I have a number of good qualities
- All in all, I am inclined to think I am a failure.
- I am able to do things as well as most other people.
- I feel I do not have much to be proud of.
- I take a positive attitude toward myself.
- On the whole, I am satisfied with myself.
- I wish I could have more respect for myself.
- I certainly feel useless at times.
- At times I think I am no good at all.

Each item is rated from Strongly Agree to Strongly Disagree on a 4-point scale (0-3).

**Chapter 3 – Behavioural diet and diet plus
physical activity interventions improve
treatment satisfaction in early Type 2
Diabetes without reducing quality of life:
Data from the Early ACTivity In Diabetes
(ACTID) Randomised Control Trial**

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Submitted to Diabetic Medicine awaiting review

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Rob Andrews provided the data on behalf of the Early ACTID trial team. I wrote the manuscript. Beverley Shields assisted with statistical analysis. All authors reviewed and edited the final manuscript.

3.1 Abstract

Aims: Diet and exercise are the cornerstone of management of Type 2 DM but 20-50% of people are non-adherent, possibly due to a reduction in wellbeing. The Early ACTID trial randomised patients to diet, diet and activity, or usual care in a 5:5:2 ratio. Patients in both intervention arms experienced improved glycaemia. We aim to assess the effects on patient-reported measures recorded, a secondary outcome of the trial.

Methods: Treatment satisfaction, quality of life, and wellbeing were assessed using five questionnaires: Diabetes Treatment Satisfaction Questionnaire (DTSQ)(n=512), EQ-5D(n=521), Brief Illness Perception Questionnaire(n=503), Rosenberg self-esteem scale(n=501) and Satisfaction with Life Scale(n=523). Analysis was performed on participants with complete data at baseline and 12 months for each questionnaire. T-tests compared mean change from baseline score between study arms.

Results: Baseline characteristics were similar; 64% vs 66% vs 68% male, median age 60.1 vs 60.4 vs 60.9 years, median days since diagnosis 184 vs 187 vs 190, mean HbA1c 48.4 vs 48.9 vs 50.3 mmol/mol, mean BMI 32 vs 31 vs 31 kg/m².

At 12 months, there was a marked improvement in DTSQ Satisfaction in those receiving a diet or diet and activity intervention compared to usual care (2.8 vs 0.5, p=0.0008 and 2.5 vs 0.5, p=0.001) There were no differences between arms in quality of life or wellbeing.

Conclusions: Diet and diet plus activity interventions in newly-diagnosed Type 2 DM improve treatment satisfaction with no adverse effect on quality of life or wellbeing. The addition of exercise to a diet program did not affect treatment satisfaction, quality of life or wellbeing.

3.2 Background

Dietary and physical activity advice form the backbone of the treatment of Type 2 DM. Both the National Institute for Health and Care Excellence (NICE) and the American Diabetes Association (ADA) advise weight loss through lifestyle changes as an essential part of the management of Type 2 DM (77,78). Better food choices, portion control and eating patterns, alongside increased physical activity and reduced sedentary time comes with numerous benefits. These include improved glycaemic control and improved cardiovascular risk factors. This is seen both with diet and exercise prescription and behavioural interventions (17,19,79).

The effects of these interventions on treatment satisfaction and quality of life are not fully understood, particularly early on in the disease when these interventions are most likely to be offered. Both the American Diabetes Prevention Program (DPP) (38) and the British DESMOND diabetes education and self-management programme (41) have looked at the effect of lifestyle interventions on quality of life in people newly diagnosed with Type 2 DM. In DPP, participants in the intensive lifestyle intervention arm (ILS) experienced a greater decline in physical function, health index and social functioning compared to both the metformin-treated and placebo-treated arms. In contrast, participants in the DESMOND study received a comprehensive diabetes self-management and education programme including lifestyle advice, and experienced a very modest decline in quality of life, similar to that seen in the control group.

Adherence to lifestyle interventions is a major issue with the Time2DoMore survey revealing adherence to dietary advice was 51% and adherence to exercise advice was just 40% (23). In a systematic review of barriers to exercise in people with Type 2 DM, dislike of exercise, sweating and physical discomfort from exercise were commonly cited as barriers (25). Similarly, in a survey of people with Type 2 DM in the USA, sticking to a diet was seen as a greater burden than taking oral glucose lowering agents (24). Both of these findings suggest that having to adhere to a healthy diet and exercise regularly may reduce wellbeing in patients with Type 2 DM as was seen in the DPP.

This research aims to assess the potential impact of behavioural lifestyle interventions on treatment satisfaction, wellbeing, and quality of life. The Early ACTivity In Diabetes (Early ACTID) trial (72) took place in the South West of England and aimed to assess whether physical activity advice given alongside dietary advice conferred significant additional benefits for people with newly diagnosed Type 2 DM. We believe patient reported measures recorded during this trial will provide strong evidence of the effects of these lifestyle changes on people with newly diagnosed Type 2 DM, and may identify associations that can be useful in predicting poor adherence and/or response to lifestyle interventions. Early ACTID had excellent retention of trial participants, achieved improvements in glycaemia in line with previous studies, and objectively measured activity levels and diet (80,81).

3.3 Participants and Methods

3.3.1 *The Early ACTID Study*

Early ACTID was a multicentre, parallel-group randomised controlled trial of lifestyle interventions which took place across five sites in South West England. The study was approved by the Bath Research Ethics Committee (05/Q2001/5), and all participants provided written informed consent. Participants were recruited through primary care with an original target sample size of 750, this was later reduced to 546 due to high retention and slower than anticipated recruitment.

The trial has previously been described (72), but in brief 593 adults diagnosed with Type 2 DM were recruited through primary care between December 2005 and September 2008. Eligible participants had been diagnosed within the previous 5–8 months and were older than 30 years at diagnosis. Exclusion criteria were age older than 80 years, HbA1c concentration greater than 10% (85.8 mmol/mol), blood pressure higher than 180/100 mm Hg, LDL cholesterol concentration higher than 4 mmol/L, body-mass index (BMI) lower than 25 kg/m², weight greater than 180 kg, use of weight-loss drugs, taking a sulphonylurea at the maximum dose, unstable angina, a myocardial infarction within the previous 3 months, inability to increase physical activity, and pregnancy or planning to become pregnant.

Participants were randomised, using a computer-generated allocation, in a 2:5:5 ratio to usual care, an intensive dietary intervention, or an intensive dietary and physical activity intervention. Randomisation was stratified by centre and minimised by age, sex, fitness, route into study and blood pressure. Allocation was performed by the trial coordinator and concealed until after Visit 4 when dietitians phoned the trial coordinator and received the allocation code. Doctors were blinded to allocation but due to the nature of intervention nurses, dietitians and participants were aware of allocation. Participants in the usual care arm received lifestyle advice at a baseline dietitian visit, and were subsequently followed up by a doctor blinded to treatment allocation at 6 and 12 months. Participants in the intensive dietary intervention arm received usual care and an additional fifteen 20 minute sessions with a nurse or dietitian. The dietary intervention was not prescriptive and targeted weight loss of 5-10% through

daily calorie reduction of 500kcal and personalised goal setting. In addition to usual care and the dietary intervention, participants in the intensive dietary and physical activity group received pedometers (Digi-Walker CW200; Yamax, Yamasa Tokei Keiki Co., Ltd., Tokyo, Japan), motivational literature, and an activity diary. In addition to their existing levels of activity, they were asked to perform 30 minutes of brisk walking at least 5 days a week. Activity levels and goals were discussed during the same session as the dietary advice in order to keep contact time the same across both interventions.

The effects of the Early ACTID interventions on glycaemia and a number of other outcomes have been previously reported (72). This analysis aims to assess the impact of the interventions on quality of life, wellbeing and satisfaction with treatment. Patient reported measures were recorded on paper copies given to participants at the 0, 6 and 12 month visits. Treatment satisfaction, quality of life, illness perception and wellbeing were assessed using five validated questionnaires.

3.3.2 Treatment Satisfaction

Diabetes-specific treatment satisfaction was assessed using the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (63). It is a disease-specific treatment assessment tool recommended by the World Health Organisation (WHO) and International Diabetes Federation (IDF). A satisfaction score is calculated from six of the questions. Questions are rated on a 7-point Likert scale (0-6, from dissatisfied to satisfied). The remaining two questions measure perceived frequency of hyper-/hypo- glycaemia and are not included in this analysis.

3.3.3 Quality of Life and Illness Perception

Health status was assessed using the Euroqol – 5 Dimensions 3 Level (EQ-5D) and Brief Illness Perception Questionnaire (BIPQ). The EQ-5D is a generic measure of quality of life recommended by the National Institute of Health and Care Excellence (NICE) (82). It is composed of 2 parts. Part one is made up of 5 items scored on 3 levels to produce a Health Index according to the population norms. Part two is a Visual Analogue Scale (VAS) where participants rate their overall health from 0-100. Each part is assessed independently.

Illness Perception was assessed using the Brief Illness Perception

Questionnaire (BIPQ). BIPQ is an abbreviated version of the Illness Perception Questionnaire (IPQ) (83). It is made up of 8 items on 11-point scales from 0-10 and a free text item on perceived cause of illness. A sum score of perceived illness threat can be created from the 8 scaled items after reversing scores for the negatively worded items.

3.3.4 Wellbeing

Wellbeing was assessed using Diener's Satisfaction with Life Scale (SWLS) and Rosenberg's Self-esteem Scale. The Satisfaction with Life Scale is composed of 5 items and assesses an individual's subjective wellbeing (59). Each item is rated on a 1-7 scale, higher scores representing increased satisfaction. It is the preferred assessment tool of subjective wellbeing as it has excellent temporal reliability, internal consistency and good convergence with other measures. Self-esteem was assessed using the Rosenberg Self Esteem Scale (RSES) (84–86). It is a 10-item questionnaire with each item rated from Strongly Disagree to Strongly Agree on a 4-point scale. Originally a Guttman Scale, we like many others have opted to score each item between 0-3, reversing the scores of negatively worded items. The sum of all 10 items provides an overall score of self-esteem.

3.3.5 Statistical Analysis

Analysis was performed using *Stata Statistical Software: Release 14* (StataCorp, TX, USA). Parametric data is given as mean and standard deviation (SD) and non-parametric data as median and interquartile range (IQR). Where participants had provided multiple responses to a question, mean question scores were used and retained in the analysis. As change scores were normally distributed, between groups comparisons were performed using unpaired t-tests of change in score between baseline and 12 months. To allow for testing of all comparisons across the 3 arms, Bonferroni correction for multiple testing meant statistical significance was achieved at $p < 0.017$. Associations were assessed using Pearson correlation coefficients. Given the minimum sample size used for comparisons in analysis is 80 vs 206, this would give us 80% power to detect a difference of 0.37 SD in our measurements. Therefore, in this study we will be well powered to detect clinically relevant effect sizes which equate to ± 2.0 for DTSQ, ± 0.07 for EQ-5D Index, ± 6.0 for EQ-5D VAS, ± 3.1 for BIPQ, ± 0.9 for

RSES, and ± 2.5 for SWLS, using the baseline questionnaire scores as a reference.

3.4 Results

Of the 579 participants that completed the trial, 545 completed at least one questionnaire in full at baseline and twelve months (range of n for analysis = 501-523) (Figure 1). Follow-up was completed in September 2009. The characteristics of participants included in this analysis are given in Table 1 and are similar to those of participants at randomisation. At baseline there was no difference between the three arms in terms of age, sex ratio, BMI, HbA1c, time from diagnosis and oral hypoglycaemic agents. Table 2 summarises the results for all questionnaires. It includes baseline scores, endpoint scores and change scores.

Table 1 - Cohort Characteristics

Baseline Characteristics Given as mean(sd) unless otherwise stated	Usual Care (n=85)	Diet (n=234)	Diet and Physical Activity (n=226)
Male Sex	54(64%)	154(66%)	154(68%)
Age in years	60.1(10.7)	60.4(10.0)	60.9(9.0)
Caucasian	83(98%)	227(97%)	214(95%)
Married or with long-term partner	64(75%)	178(76%)	180(80%)
Median (IQR) days since diagnosis	184(149-223)	187(153-225)	190(149-233)
BMI	32(5.0)	31(5.8)	31(5.1)
HbA1c (%)	6.6(0.9)	6.6(0.9)	6.8(1.0)
HbA1c (mmol/mol)	48.4(9.7)	48.9(10.0)	50.3(11.4)
Minutes of moderate to vigorous activity per day	26.9(21.0)	25.8(19.6)	23.3(18.3)
Oral hypoglycaemic agents <ul style="list-style-type: none"> Metformin Sulphonylurea Thiazolidinedione Total 	25(29%) 6(7%) 2(2%) 28(33%)	83(35%) 19(8%) 1(<1%) 91(39%)	77(34%) 20(9%) 3(1%) 87(38%)
Antihypertensive agent	50(59%)	159(68%)	129(57%)
Lipid-lowering drugs	55(65%)	152(65%)	141(62%)
Antiobesity agents	0	0	0

Figure 1 - CONSORT diagram

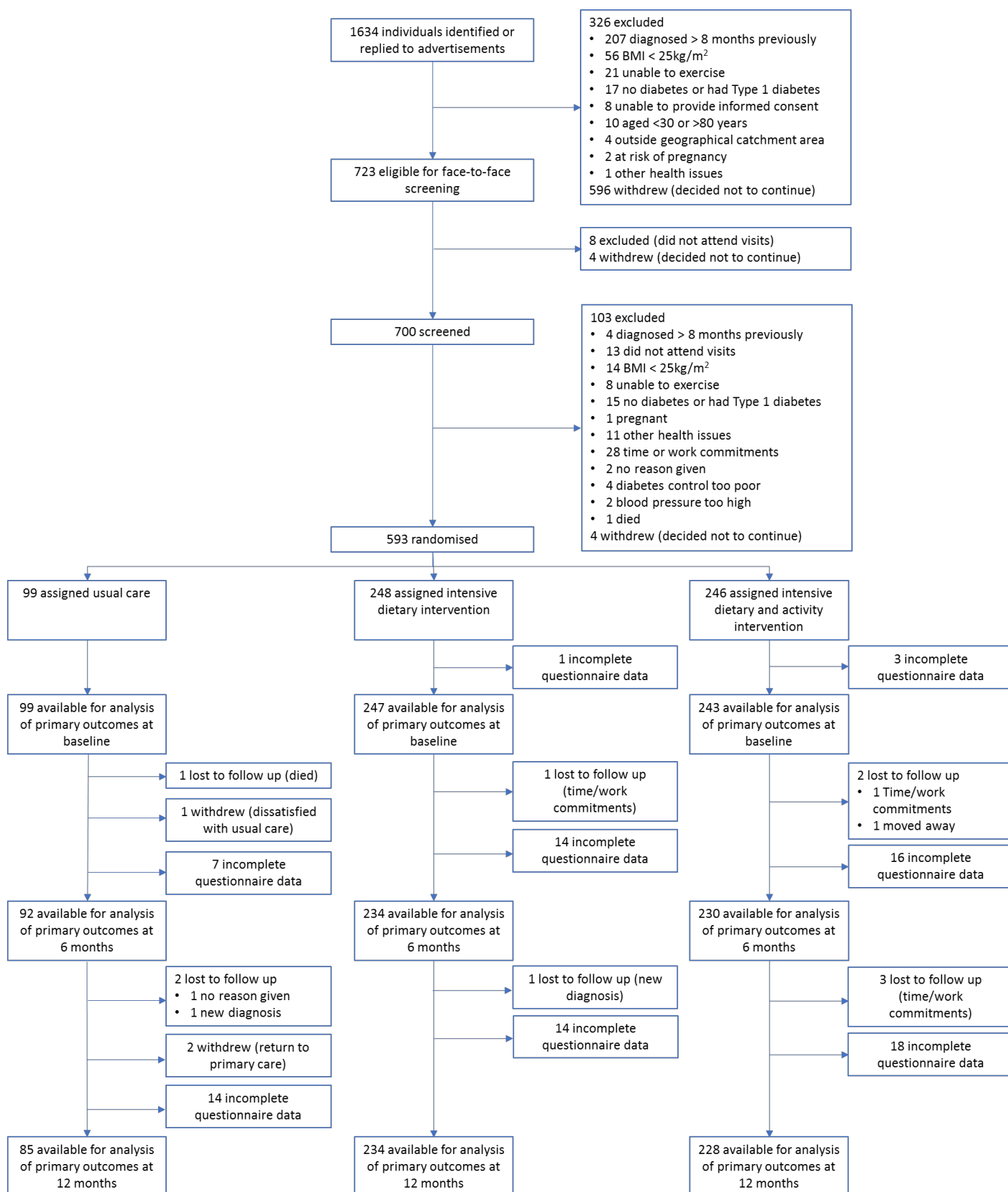


Table 2 – Summary of Questionnaire Results. Baseline and 12 month results are given as median (IQR). 12 month change scores are given as mean (SD). T-tests were used to compare means and Mann-Whitney U Tests to compare medians. Statistical significance was achieved at $p < 0.017$ after Bonferroni correction, *denotes statistical significance.

	Trial Arm			P values		
	Usual Care	Diet	Diet and Physical Activity	Usual Care vs Diet	Usual Care vs Diet and Physical Activity	Diet vs Diet and Physical Activity
Diabetes Treatment Satisfaction Questionnaire (DTSQ) (maximum score 36)						
N	83	216	213			
Baseline	32(26-35)	31(27-34)	31(27-34)	0.3	0.6	0.5
12 months	31(28-35)	33.5(30-35)	34(31-36)	0.01*	0.007*	0.6
12 month Change	0.53(5.23)	2.82(5.24)	2.46(4.36)	0.0008*	0.001*	0.4
EQ-5D Health Index (maximum score 1)						
N	81	223	217			
Baseline	0.80(0.73-1)	0.80(0.73-1)	0.88(0.73-1)	0.6	0.05	0.03
12 months	0.80(0.69-1)	0.85(0.73-1)	0.85(0.73-1)	0.02	0.005*	0.5
12 month Change	-0.05(0.23)	0.00(0.15)	-0.02(0.15)	0.03	0.2	0.2
EQ-5D Visual Analogue Scale (EQ-5D VAS) (maximum score 100)						
N	82	222	215			
Baseline	75(62-85)	75(65-85)	79(65-85)	0.7	0.3	0.4
12 months	75(66-80)	80(70-85)	80(70-90)	0.03	0.01*	0.5
12 month Change	-0.62(16.3)	2.87(14.6)	2.40(16.8)	0.07	0.2	0.8
Brief Illness Perception Questionnaire (BIPQ) (maximum score 80)						
N	80	217	206			
Baseline	44(39-51.5)	46(41-52)	44.5(40-49)	0.2	0.9	0.07
12 months	45(38-50.5)	45(41-51)	45(41-50)	0.1	0.2	0.5
12 month Change	-0.49(6.30)	0.14(6.57)	0.75(6.82)	0.5	0.2	0.3
Rosenberg's Scale of Self-Esteem (RSES) (maximum score 30)						
N	80	214	207			
Baseline	20(18-22)	20(18-22)	20(18-22)	0.7	0.5	0.8
12 months	20(18-22)	21(18-22)	20(18-23)	0.2	0.1	0.8
12 month Change	-0.20(2.13)	0.17(2.08)	0.17(2.73)	0.2	0.3	0.9
Satisfaction with life scale (SWLS) (maximum score 35)						
N	78	226	219			
Baseline	23(16-29)	25(20-29)	26(20-30)	0.06	0.03	0.7
12 months	22(18-29)	27(20-30)	26(20-30)	0.02	0.001*	0.8
12 month Change	0.37(6.15)	0.40(4.81)	0.50(4.69)	1.0	0.8	0.8

3.4.1 Treatment Satisfaction

Intensive dietary intervention with and without physical activity advice improved treatment satisfaction compared to usual care (Fig. 2). Participants receiving the intensive dietary intervention had a mean (SD) improvement in satisfaction score of 2.8 (5.2) compared to usual care 0.5 (5.2) ($p=0.0008$). In addition, those who received intensive dietary and physical activity advice improved by 2.5 (4.4) compared to the 0.5 (5.2) improvement in usual care ($p=0.001$). However, the addition of physical activity advice did not provide a greater increase in treatment satisfaction than when dietary advice was given alone ($p=0.4$). This was despite high baseline treatment satisfaction across all treatment arms with median (IQR) scores of 32 (26-35), 31 (27-34) and 31 (27-34). At 6 months, treatment satisfaction improved in all arms, with mean (SD) change of; 1.0 (4.5) in the usual Care arm, 2.6 (5.8) in the diet arm, and 1.78 (4.7) in the diet and activity arm. There was no statistically significant difference between arms ($p>0.03$).

The largest improvements were seen in the understanding and satisfaction items (Fig. 3). The understanding component of DTSQ asks patients *“How satisfied are you with your understanding of your diabetes?”* Participants in the intensive dietary intervention and intensive dietary and physical activity intervention arms both had a mean improvement of 0.6 in this component. Participants receiving usual care improved by just 0.2. In addition, the satisfaction component of DTSQ asks patients *“How satisfied are you with your current treatment?”* and both intervention arms had mean improvements of 0.6 and 0.5 in this component, compared to a modest improvement of 0.1 in the usual care arm.

Figure 2 – Mean (95% CI) change from baseline Diabetes Treatment Satisfaction Questionnaire (DTSQ) Satisfaction Score

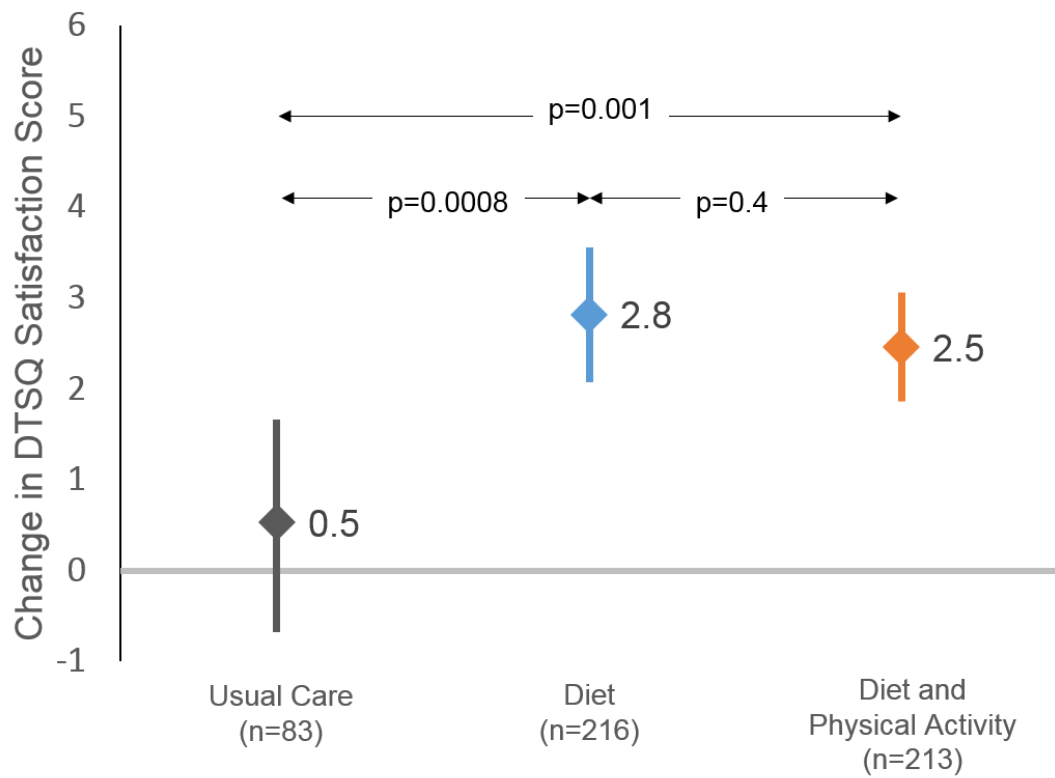
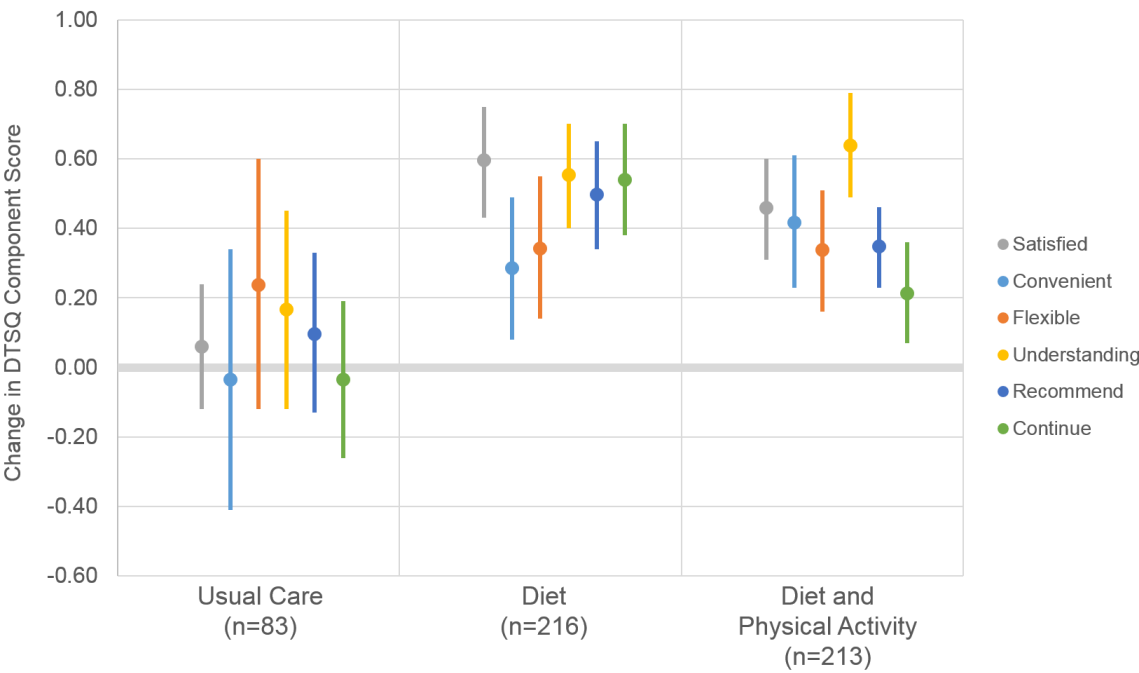


Figure 3 – Mean (95% CI) change from baseline score at 12 months in Diabetes Treatment Satisfaction Questionnaire (DTSQ) Components of Satisfaction Score



3.4.2 Quality of Life, Illness Perception, and Wellbeing

Quality of life, illness perception and wellbeing were unchanged after 12 months across all trial arms. There were no between arm differences in mean change in any of these measures. Non parametric comparison of raw scores at 12 months showed a small statistically significant difference in 12 month median EQ-5D Index between both intervention arms and control (Usual Care 0.80 vs Diet 0.85, $p=0.015$; Usual Care 0.80 vs Diet and Activity 0.85, $p=0.005$). However, there was no difference in mean change from baseline score ($p=0.03$ and $p=0.2$ respectively), There was also a small statistically significant difference between the usual care and the diet and activity arms of the trial in 12 month median EQ-5D VAS (75 vs 80, $p=0.01$) and SWLS (22 vs 26, $p=0.001$) but again no difference in mean change from baseline (-0.62 vs 2.40 , $p=0.2$; 0.37 vs 0.50 , $p=0.8$).

Baseline life satisfaction, self-esteem and quality of life were not predictive of response to treatment in terms of weight or glycaemia. Pearson correlation R values were all ≤ 0.1 with no correlations reaching statistical significance.

3.5 Discussion

In this study, we have shown that motivational interview-based behavioural diet and diet plus physical activity interventions improved treatment satisfaction in early Type 2 DM. Quality of life, illness perception and wellbeing were all stable over the course of the trial across all arms and no different between arms. None of the patient reported measures recorded in this study were associated with a change in weight or glycaemia in the intervention or control arms. These findings suggest that an individual's quality of life and/or wellbeing is not altered by, or has an effect on, the impact of a diet or diet plus physical activity intervention. This suggests that poor adherence to lifestyle programmes is not due to them having adverse effects on quality of life and/or wellbeing. It also underlines that these programmes are effective for patients who have low psychological wellbeing or high levels of stress about their disease.

We were not surprised to see an improvement in diabetes treatment satisfaction in the diet and diet and activity arms. Improvement in treatment satisfaction was seen in the intervention arm of the Diabetes X-PERT study in which patients with established Type 2 DM attended six 2 hour sessions of self-management education (67). Similar improvements have been seen in studies of long acting and rapid acting insulins, incretin-related agents, sodium-glucose cotransporter 2 (SGLT2) inhibitors, fixed-dose combination tablets and dipeptidyl peptidase-4 (DPP-4) inhibitors (65). The improved glycaemic control, weight loss, and reduced need for drug treatment seen in both intervention arms were probably the reasons for the improvement in Diabetes treatment satisfaction (72). The fact that the improvement in these factors was no different between the two intervention arms also probably explains why no difference in treatment satisfaction was seen between the intervention arms.

Only two studies have assessed the impact of behavioural lifestyle interventions on wellbeing and quality of life in newly diagnosed Type 2 DM. The DPP found that in individuals who were diagnosed with Type 2 DM, those in the intense lifestyle intervention (ILS) arm had a greater fall in quality of life than those in the metformin or control arm over up to six years of follow up (38). Whether this was due to them having experienced more intense disappointment when, in spite of actually losing weight, they still developed diabetes or due to the fact that the intervention was very intense, prescriptive and involved making

significant changes in their diet and patterns of physical activity is not known. In contrast, in the DESMOND study, participants who received the intervention experienced a very modest decline in quality of life, similar to that seen in the control group (41). The intervention used in the DESMOND study was similar to that used in ACTID, being a non-supervised intervention that emphasised patient understanding and self-management and had total contact time of 6 hours.

The diet and diet and activity interventions only produced a - 2.41kg (95% CI - 3.49 to -1.32; $P<0.0001$) and - 2.25kg (95% CI -3.35 to -1.16; $P<0.0001$) weight loss compared to the usual care arm which might not have been enough to have an effect on wellbeing or quality of life. A review of the relationship between weight loss and health related quality of life suggested that improvements were only seen if weight loss was significant (87). In the DiRECT study, a randomised control trial of an intense weight management programme in patients with established Type 2 DM, a weight loss of -8.8kg (95% CI -10.3 to -7.3; $p<0.0001$) was seen compared to the usual care group (22). In this study quality of life, as measured by the EQ5D VAS, improved by 6.4 points (95% CI 2-5 to 10.3; $p=0.012$) in the weight management arm compared to the usual care arm.

It was disappointing not to see a difference in wellbeing and quality of life between the diet and diet and activity arms. It is difficult to know if increasing activity levels more than the 9.1 (95% CI 4.45 to 13.75; $p=0.036$) minutes per day that was achieved in the diet and activity arm would have resulted in an improvement in wellbeing and/or quality of life. DESMOND and the DPP did not objectively measure activity and the small exercise focused studies found mixed effects on wellbeing and quality of life and could not establish a threshold of effect (44). Similarly, whether adding an anaerobic component to the diet and activity arm, (the exercise focus was on increasing aerobic activity) would have resulted in an improvement in wellbeing and/or quality of life is not known. The small studies that have compared the effect of different forms of exercise on quality of life and wellbeing have not been able to determine whether one type or combinations of types of exercise are better (44).

Our study had several strengths. First, it included well-validated measures of treatment satisfaction, quality of life, and illness perception. Second, the three-

arm design allowed for direct comparison between a behavioural dietary intervention given alone and when delivered in combination with a behavioural physical activity intervention. Third, excellent retention meant 545 of 593 (92%) participants at randomisation completed at least one questionnaire in full at both baseline and 12 months, with at least 501 results available for each questionnaire analysis. This provides us with confidence our study was adequately powered to detect clinically significant changes in each measure. In addition, Early ACTID objectively measured diet and activity levels which allowed us to ensure that participants receiving the intervention had indeed changed their diet and activity levels.

There are also limitations worth noting. First, the study participants were not ethnically diverse with 96% Caucasian. A more diverse ethnic group might have resulted in different findings. Second, the unblinded nature of the trial (i.e., to participants and study staff) may have influenced participant expectations about the efficacy of the intervention to which they were assigned. Third, using the Diabetes Treatment Satisfaction Questionnaire change version with the original Treatment Satisfaction Questionnaire may have enabled us to explore in more detail the improvement that patients saw with the intervention arms (73,88). Finally, the absolute improvement in HbA1c and weight loss were modest in both intervention arms. Had there been greater improvement in these, we might have seen changes in quality of life and wellbeing in the intervention arms.

In summary, we have found that motivational interview-based behavioural diet and diet plus physical activity interventions improved treatment satisfaction in early Type 2 DM without adversely impacting wellbeing and quality of life. In addition, quality of life and wellbeing were not associated with response to these interventions. However, what we aren't able to say from our results is whether these interventions are able to prevent or delay decline in quality of life. Evidence from the usual care arm suggests that quality of life is stable in newly diagnosed Type 2 DM, but this was in a trial environment where participants received "enhanced" usual care. Future work on the impact of lifestyle changes in newly diagnosed Type 2 DM should consider looking at changes in quality of life in prospective studies instead of interventional trials. To aid this work further, standardisation of patient reported measures used in future studies should be a priority as currently work in this area is made difficult by the large variation in

different measures used (89,90). This makes cross-comparison difficult and prevents meta-analysis of studies from which stronger conclusions can be drawn.

Chapter 4 – Quality of life declines over the first six years following diagnosis of Type 2 diabetes, but wellbeing is stable: Data from Early ACTID and ACTID Plus

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Rob Andrews provided the data on behalf of the Early ACTID trial team. I wrote the manuscript. Beverley Shields and John Dennis assisted with statistical analysis. Richard Oram, Rob Andrews and I reviewed and edited the final manuscript.

4.1 Abstract

Background and aims: People living with Type 2 Diabetes (T2DM) report poorer quality of life than those without the disease. It is not clear whether there is a fall in quality of life due to being diagnosed with T2DM or whether this falls over time due to living with the disease. Some studies have shown quality of life declines initially at diagnosis but then returns to its previous level but the DPPOS found it declined over 6 years of follow up. In this study we aimed to assess quality of life, treatment satisfaction and wellbeing in a cohort with recently diagnosed T2DM in the United Kingdom over 6 years.

Materials and methods: The cohort we used were participants enrolled in the Early ACTID Trial. Participants with newly-diagnosed Type 2 diabetes were randomised to a 1 year diet intervention, a 1 year diet and activity intervention, or usual care in a 5:5:2 ratio. At the end of the year participants' care was returned to their general practitioner and they were seen annually for a further 5 years. Patient-reported measures (PRMs) were recorded at 0, 6, 12, 24, 36, 48, 60, 72 months; these were EQ-5D, BIPQ, DTSQ, RSES, and SWLS. Analysis was performed using mixed effects linear regression to allow for clustering of results within individuals.

Results: Baseline cohort characteristics were: 64% male, median age 60 years, median time since diagnosis 189 days, mean HbA1c 49.8 mmol/mol, mean BMI 31.6. At baseline 589 of 593 (99%) participants completed at least one questionnaire in full. This fell across the study with 551 (93%) at year 1 and 290 (49%) at year 6. Health status declined gradually over six years irrespective of trial arm. Those whose diabetes progressed during the trial had poorer quality of life than those who progressed during follow up (-0.5, 95% CI 0.01, 0.09; $p=0.009$). Perceived illness threat fell across the six years (-0.2, $p=0.005$), this was lowest in participants whose diabetes did not progress but was not statistically significant (-1.3, $p=0.2$).

Conclusion: Quality of life of declines gradually over the first six years of Type 2 diabetes. This decline appears to be associated with progression of diabetes though further clarification is required. Participants' perception of illness threat decreased slowly, suggesting they came to terms with the impact of their illness, particularly in those whose disease did not progress. Wellbeing was stable although depression was not assessed.

4.2 Background

Quality of life is a hugely important outcome in healthcare. Although various definitions exist it can be described well as “a multi-faceted construct that encompasses the individual’s behavioural and cognitive capacities, emotional well-being and abilities requiring the performance of domestic, vocational and social roles” (91). Its importance in Type 2 Diabetes (Type 2 DM) is increasingly highlighted (92).

Those with Type 2 DM report poorer quality of life than those without the disease (30,93). This quality of life falls further if the person has macrovascular or microvascular complications, depression, or is taking more than 7 tablets (39,40). Level of long term glucose control (HbA1c) and which treatment is used to treat diabetes does not affect quality of life (5,6).

It is less clear what changes in quality of life occur in newly diagnosed diabetes prior to the development of complications. Early research suggested a dip around the time of diagnosis that quickly returned to its previous level (35–37,94). The American Diabetes Prevention Program Outcomes Study (DPPOS) followed quality of life in those people in whom diabetes was diagnosed despite the interventions (38). Quality of life declined over six years irrespective of trial arm. However, it is not known whether this is the same in people who were not made aware of their risk and developed diabetes despite efforts to prevent it.

Our cohort is composed of the participants of the Early ACTivity In Diabetes (Early ACTID) randomised control trial and its follow up study ACTID Plus. Early ACTID aimed to determine whether the addition of physical activity advice to dietary advice conferred an additional benefit above dietary advice alone in newly diagnosed Type 2 DM. After completion of the interventions at 1 year, there was improved treatment satisfaction in the intervention groups but there was no change in health status, life satisfaction, self-esteem and illness perception and no difference between arms (Chapter 3). Following this, participants were re-consented to the follow up study ACTID Plus which followed participants annually for a further 5 years. In this study we use patient reported outcome measures recorded during the trial, and at each follow up visit, to analyse changes in these measures over time. This study also aims to identify

whether progression of diabetes was associated with changes in these measures.

4.3 Participants and Methods

4.3.1 Cohort & Measures Used

Our cohort is composed of the participants of the Early ACTID randomised control trial and its follow up study ACTID Plus. Funding for ACTID plus was delayed which meant that some people had gone past their 1st year of follow up before the follow up started. For this reason there is more missing data at the first year of follow up (2 years post-randomisation). This is described in full in Chapter 2.

The measures we used are also described in Chapter 2.

Progression of diabetes was a binary survival outcome defined by an increase in HbA1c of >5 mmol/mol or the addition of ≥ 1 diabetes medication(s).

4.3.2 Statistical Analysis

All analysis was performed using *Stata Statistical Software: Release 14* (StataCorp, TX, USA). Longitudinal analysis of each patient-reported outcome measure was performed using mixed effects linear regression modelling. Models were adjusted for Early ACTID trial arm, age, sex and BMI. Analysis of the association between each patient-reported outcome measure and diabetes progression was also performed using mixed effects linear regression. For this analysis, participants were categorised according to whether their disease; progressed during the trial, progressed during follow up, or did not progress. Those with missing progression data were excluded from this analysis.

4.4 Results

4.4.1 *Baseline Characteristics*

Of 593 enrolled participants, 589 had complete data for at least one patient reported outcome measure at baseline. The number of individuals who completed at least one measure in full at 6, 12, 24, 36, 48, 60, and 72 months was 542, 551, 193, 298, 316, 286, and 290. Baseline cohort characteristics for all individuals included in the analysis, those with complete for at least one measure at years, and those without data at 6 years are given in Table 1. There were small differences in age, sex and BMI between individuals with 6 year data and those without, but otherwise baseline clinical characteristics were similar. Importantly, baseline patient reported outcome measures were similar between these two groups. The main results of this study are displayed in Figure 1. Results split by trial arm are shown in Table 2. Results with participants categorised by time of diabetes progression are displayed in Figure 2. Figure 3 displays linear trends seen in EQ-5D Index.

4.4.2 *Quality of Life*

There was a very gradual decline in EQ-5D Index (-0.01 per year, $p < 0.001$) and at six years this represented a clinically significant reduction in health status with a reduction of -0.06 between baseline and 6 years ($p < 0.001$). This did not differ between treatment arms.

There was very modest decline EQ-5D VAS, with an annual decline of -0.4 ($p = 0.002$) and change of -2.1 from baseline to 6 years ($p = 0.03$). There were no significant differences between arms.

Categorising participants by their time of progression and modelling their trajectories at each time point suggested those who progressed within the trial had poorer quality of life than the rest of the cohort (Figure 2). The rest of the cohort was divided into those whose diabetes progressed during follow-up, and those who did not progress.

To investigate this further we modelled time as a continuous variable (Figure 3). We found scores in those who progressed during the trial were significantly lower than those who progressed during follow up (-0.5, 95% CI 0.01, 0.09, $p = 0.009$), but not statistically significantly different to those who did not

progress (-0.4, 95% CI -0.01, 0.09; $p=0.09$). The annual rate of decline (-0.01, 95% CI -0.02, 0.00; $p=0.007$) did not differ between the categories ($p=0.7$ & 0.9).

4.4.3 Illness Perception

There was a modest decline in perceived illness threat measured by BIPQ sum score. The annual decline was -0.2 ($p=0.005$) with a reduction of -0.9 from baseline to six years. There were no significant differences between trial arms.

Those whose diabetes did not progress over the six years of follow up had a greater reduction in perceived illness threat compared to those in whom diabetes progression was seen (Figure 3). However, these differences were not statistically significant. Compared to those who progressed during the trial this difference was 1.3 (95% CI -0.6, 3.3; $p=0.2$) and compared those who progressed during follow up was 1.3 (95% CI -0.5, 3.1; $p=0.2$).

4.4.5 Global Life Satisfaction and Self Esteem

Self-esteem was stable over the course of the study (annual trend +0.05, $p=0.004$). This resulted in a difference of just 0.3 between baseline and six years. There was no statistically significant difference between trial arms.

Global life satisfaction remained remarkably stable over the course of the study with no significant annual trend ($p=0.4$) or difference between baseline and six years ($p=1$).

Self-esteem was higher in those whose diabetes did not progress compared to those who progressed during the trial but the effect size was small (0.65, 95% CI 0.0, 1.3; $p=0.04$). Life satisfaction was significantly lower in those who progressed during the trial than those who did not progress but this was likely due to a large baseline difference (-2.7, 95% CI -4.3, 1.0; $p=0.002$).

4.4.6 Treatment Satisfaction

Treatment satisfaction improved rapidly during the one year of Early ACTID with a mean modelled annual increase of 1.0 ($p<0.001$). However, after participants stopped receiving the interventions these values quickly returned to their original level (-0.4 annual trend, $p<0.001$). Both intervention arms improved significantly greater than those in the usual care between baseline and one year but there was no difference between arms from one year to six years.

Table 1 – Baseline cohort characteristics for individuals who completed questionnaires out to six years and those who did not.

Baseline Characteristics	Cohort with baseline data	Cohort with 6 year data	Cohort without 6 year data
Proportion of trial cohort (%)	589 (99%)	290 (49%)	303 (51%)
Proportion allocated Usual care (%)	99 (100%)	38 (38%)	61 (61%)
Proportion allocated Diet (%)	247 (99.5%)	123 (50%)	125 (50%)
Proportion allocated Diet and activity (%)	243 (99%)	129 (52%)	117 (48%)
Proportion Caucasian (%)	582 (96%)	281 (99%)	282 (93%)
No. male (%)	379 (64%)	207 (71%)	174 (57.4%)
Mean Age (sd)	59.9 (10.2)	61.0 (8.9)	59.0 (11.1)
Mean BMI (sd)	31.6 (5.7)	30.9 (5.4)	32.4 (5.9)
Mean baseline HbA1c % (sd)	6.7 (1.0)	6.6 (0.9)	6.8 (1.0)
Mean baseline HbA1c mmol/mol (sd)	49.8 (11.0)	49.0 (10.3)	50.3 (11.4)
Median days since diagnosis at baseline (iqr)	189 (152-230)	187 (153-226)	190 (150-233)
Mean daily minutes of MVPA (sd)	24.8 (19.0)	25.3 (19.5)	24.1 (18.4)
Median baseline EQ-5D Index (IQR)	0.85 (0.73-1)	0.85 (0.73-1)	0.85 (0.73-1)
Median baseline EQ-5D VAS (IQR)	75 (65-85)	75.5 (65-85)	75.5 (65-85)
Median baseline SWLS Score (IQR)	25 (19-29)	26 (20-29)	24 (18-29)
Median baseline RSES Score (IQR)	20 (18-22)	20 (18-22)	20 (18-22)
Median baseline BIPQ Score (IQR)	46 (40-52)	46 (41-52)	45 (41-52)
Median baseline DTSQ Score (IQR)	31 (26-34)	32 (27-34)	30(26-34)

Table 2 – Model baseline-endpoint contrasts and annual trends split by trial arm

	Usual Care	Diet	Diet and Activity
EQ-5D Health Index (scores range from -0.594 to 1)			
Year 6 vs Baseline	-0.06 (-0.1, 0.00), p=0.04	-0.06 (-0.1, -0.03), p<0.001	-0.05(-0.08, -0.02), p=0.003
Annual Trend	-0.01(-0.02, -0.01), p<0.001	-0.01(-0.01, 0.00), p<0.001	-0.01(-0.01, 0.00), p=0.001
EQ-5D Visual Analogue Scale (scores range from 0 to 100)			
Year 6 vs Baseline	-3.3(-8.6, -2.0), p=0.2	-2.7(-5.7, 0.3), p=0.08	-1.2(-4.1, 1.8), p=0.4
Annual Trend	-1.0(-1.7, -0.3), p=0.004	-0.5(-0.9, 0.0), p=0.03	-0.2(-0.6, 0.2), p=0.3
Brief Illness Perception Questionnaire (scores range from 0 to 80)			
Year 6 vs Baseline	-1.6(-3.9, 0.7), p=0.2	-1.3(-2.6, 0.0), p=0.06	-0.3(-1.6, 1.0), p=0.7
Annual Trend	-0.3(-0.6, 0.0), p=0.05	-0.2(-0.3, 0.0), p=0.09	-0.2(-0.3, 0.0), p=0.09
Satisfaction with Life Scale (scores range from 5 to 35)			
Year 6 vs Baseline	0.8(-0.9, 2.5), p=0.4	0.7(-0.3, 1.6), p=0.2	-0.3(-1.2, 0.7), p=0.5
Annual Trend	-0.2(-0.4, 0.1), p=0.2	0.1(-0.1, 0.2), p=0.4	-0.01(-0.1, 0.0), p=0.9
Rosenberg Self-Esteem Scale (scores range from 0 to 30)			
Year 6 vs Baseline	-0.1(-0.8, 0.6), p=0.7	0.3(-0.1, 0.7), p=0.5	0.6(0.2, 0.9), p=0.006
Annual Trend	-0.08(-0.2, 0.0), p=0.1	0.05(0.0, 0.1), p=0.07	0.1(-0.1, 0.1), p=0.9
Diabetes Treatment Satisfaction Questionnaire (scores range from 0 to 36)			
Year 6 vs Baseline	0.06 (-1.7, 1.8), p=0.9	0.4 (-0.6, 1.4), p=0.4	0.6 (-0.4, 1.6), p=0.2
Annual Trend Year 0-1 (trial)	0.4 (-0.3, 1.1), p=0.3	1.0 (0.5, 1.4), p<0.001	1.2 (0.7, 1.7), p<0.001
Annual trend Years 1-6 (follow up)	-0.5 (-0.7, -0.2), p<0.001	-0.5 (-0.6, -0.3), p<0.001	-0.3 (-0.5, -0.2), p<0.001

Figure 1 - Longitudinal trends in questionnaire scores with time as discrete events; (A) Health Status measured by EQ-5D Index, (B) perception of health measured by EQ-5D VAS, (C) perceived illness threat measured by BIPQ, (D) life satisfaction measured by SWLS, (E) self-esteem measured by RSES, and (F) treatment satisfaction measured by DTSQ.

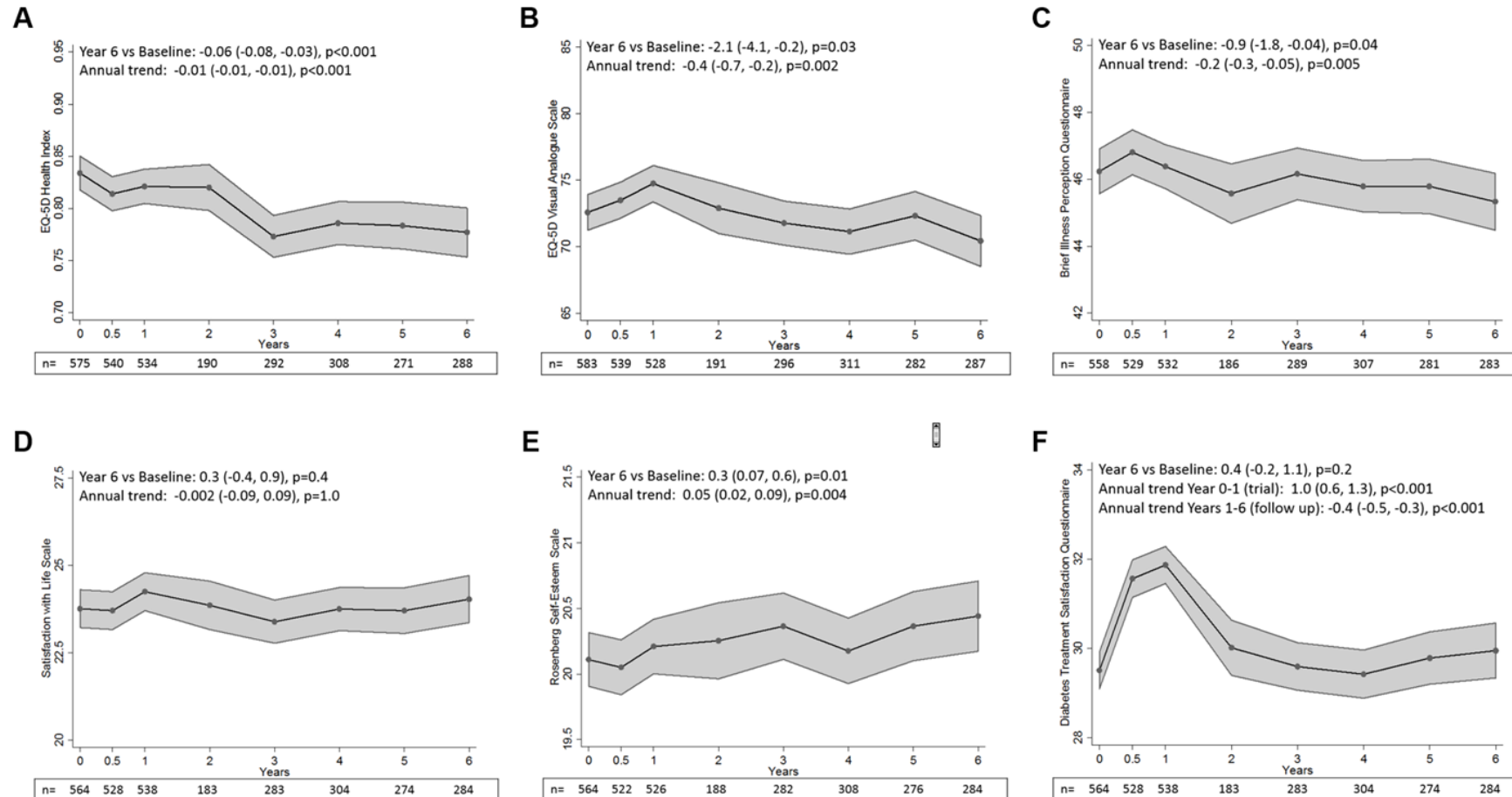


Figure 2 – Longitudinal trends in questionnaire score with time as discrete events, categorised by time of diabetes progression; (A) Health Status measured by EQ-5D Index, (B) perception of health measured by EQ-5D VAS, (C) perceived illness threat measured by BIPQ, (D) life satisfaction measured by SWLS, (E) self-esteem measured by RSES, and (F) treatment satisfaction measured by DTSQ.

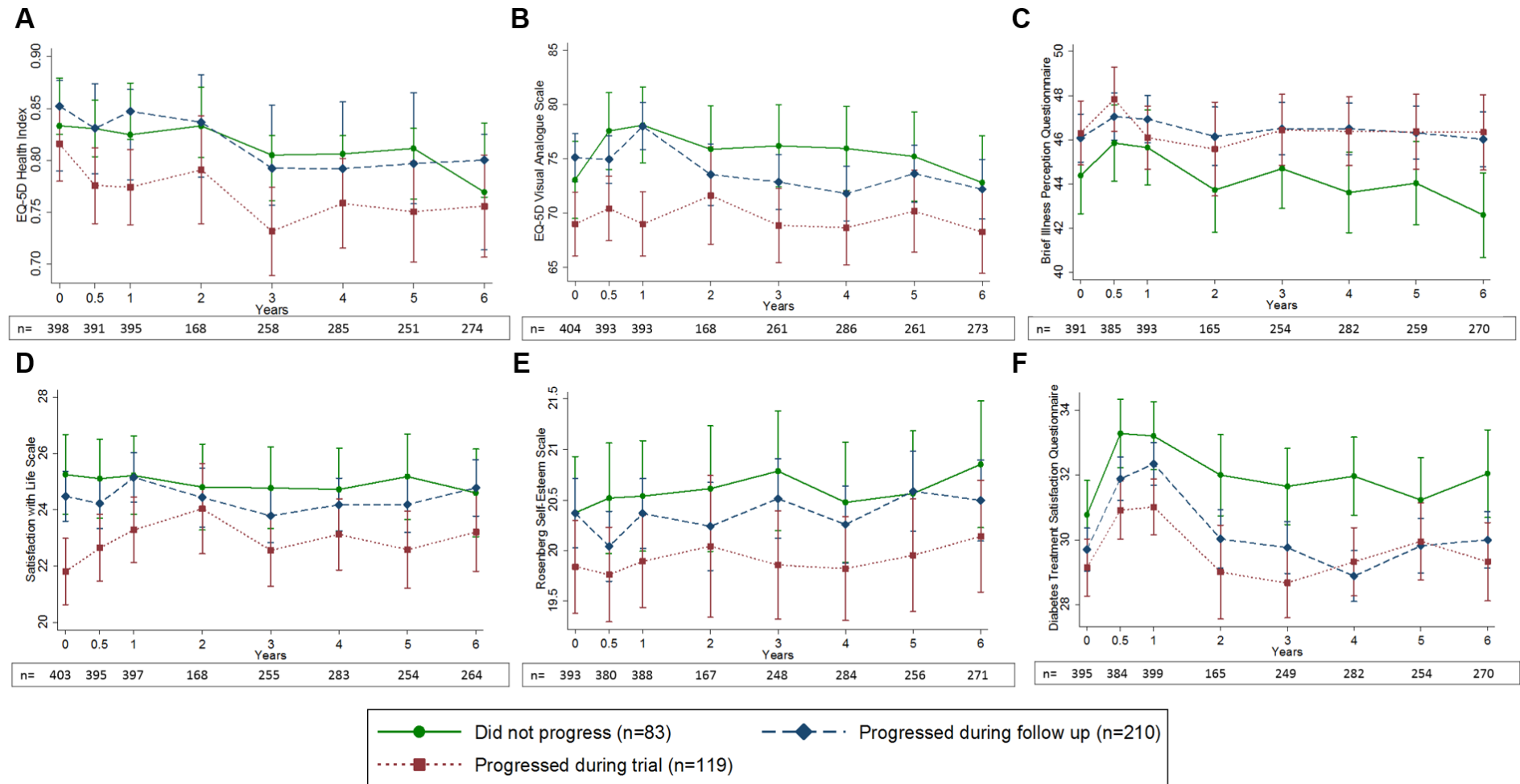
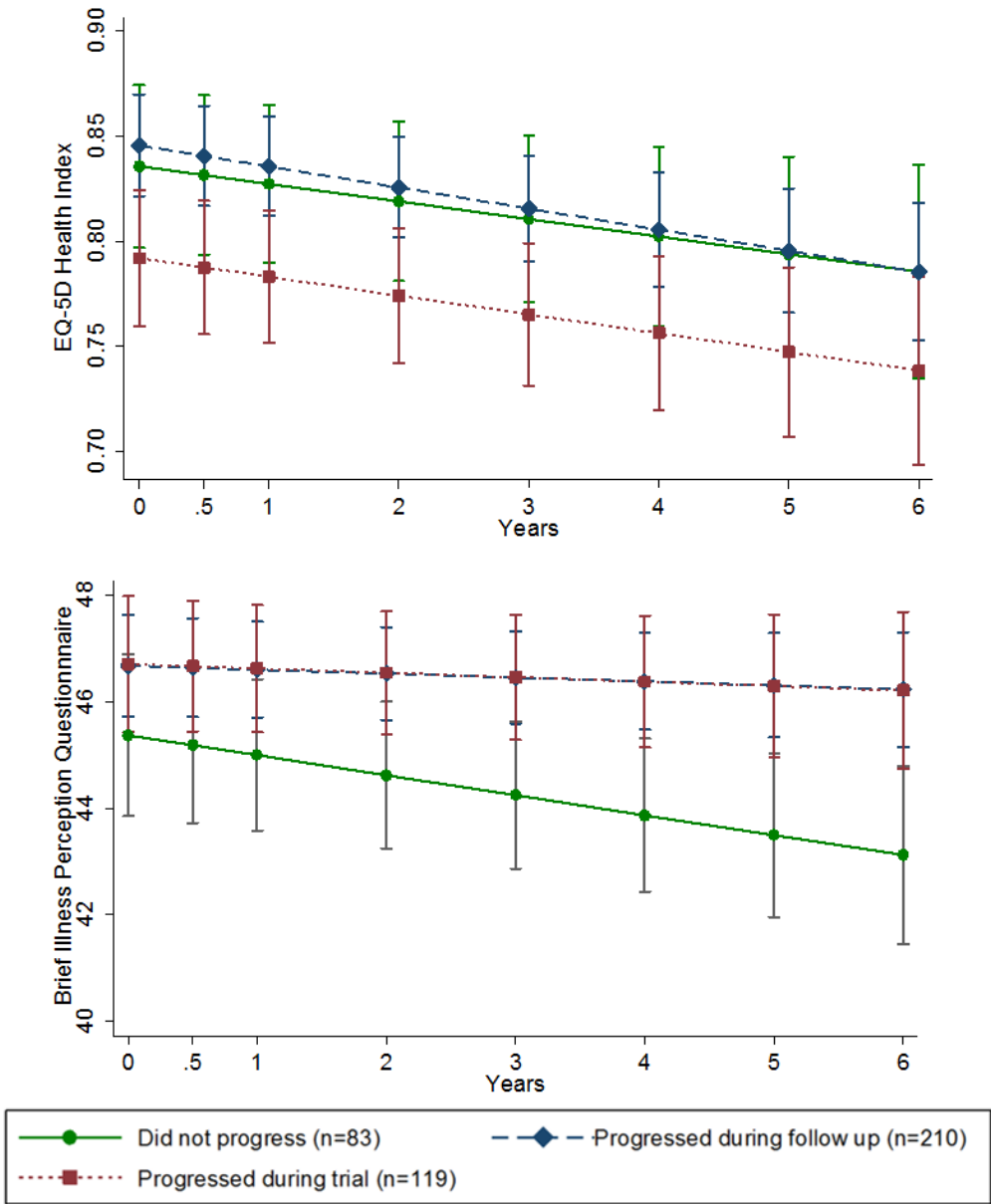


Figure 3 – Longitudinal trends in questionnaire scores with time as continuous variable; (A) Health status measured by EQ-5D Index, and (B) perceived illness threat measured by BIPQ



4.5 Discussion

In this study we found health status as measured by EQ-5D Index declined slowly over the six years following diagnosis and this represented a significant decline. Declines in EQ-5D VAS score and BIPQ sum score of illness threat were also seen but these were modest and did not reach a level considered clinically significant. We also found people who had progression of their diabetes during the trial had lower quality of life than both those who progressed during follow up and those who did not progress. Those who did not have progression of their diabetes had lower perceived illness threat. These results are important as they suggest preventing progression of diabetes through early lifestyle interventions is vital to delaying or preventing the decline in quality of life seen over this period.

The decline in health status that we saw in this study over the six years was in keeping with previous studies. Early studies suggested there was dip in quality of life at the time of diagnosis but this quickly returned to its previous level (35–37). The American Diabetes Prevention Program Outcomes Study (DPPOS) presented a unique opportunity to assess the impact of diagnosis on quality of life (38). Participants who despite the interventions went on to develop diabetes were followed for up to 6 years following diagnosis. Quality of life was measured using the SF-36 generic measure of health related quality of life. Physical component summary scores fell in all trial arms in those with diabetes and mental component summary scores fell in the lifestyle intervention (ILS) arm. This fall could have been due to them feeling disheartened to have developed Type 2 DM despite their best efforts, as a result of the number of lifestyle changes that they were being asked to make or alternatively due to progression of their diabetes. Our results suggest this decline was a normal part of the progression of Type 2 DM over this period.

The fact we saw a significant decline in EQ-5D Index but only a very modest decline in EQ-5D VAS is intriguing. This is likely be due to the fact EQ-5D VAS incorporates individuals' perception as well as functional status as it asks individuals to place on a line from 0-100 their perceived health state. This is not the case for EQ-5D Index which is restricted to five domains. The fact we also

saw a concurrent decline in perceived illness threat might explain why the EQ-5D VAS did not fall as much as the EQ-5D.

Our finding that perceived illness threat fell over time is in keeping with other studies in this area which have shown perceived illness threat is low in newly diagnosed diabetes, prior to the development of complications (41,95,96). Participants in the Early ACTID study, irrespective of the arm that they were allocated to, received enhanced care with the usual care arm being seen 11 times across the year and those in the interventions arms 17 times. This increased contact may have increased their understanding of their disease and this reduced how threatening they saw their disease. In the Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND) study, reduced illness threat was also seen as measured by the Revised Illness Perception Questionnaire (IPQ-R). They found illness understanding and personal control were higher in the intervention compared to the control group up to three years post-intervention.

By categorising participants according to their time of diabetes progression, our results suggest those whose diabetes progressed during the trial had the poorest quality of life. Although this difference was only statistically significant when compared to those who progressed during the trial, likely due to the larger numbers in this group. This may have been due to participants' disappointment at having not achieved better control through lifestyle changes, or may be the result of poorer self-efficacy, self-care and adherence to treatment. In contrast, those whose diabetes did not progress over the six years of follow up perceived their illness to be less threatening, than those whose diabetes progressed at any point during follow up. These results suggest preventing early progression of diabetes through lifestyle changes may prevent or delay the decline in quality of life normally seen in the first years following diagnosis of Type 2 DM.

We were surprised to see no difference in quality of life or wellbeing between the treatment arms and the control group over time. The interventions as well as being designed to help people to improve their diet and increase their activity, also provided them with education about diabetes and skills to overcome barriers and prevent relapse. By doing this we hoped that participants would be able to maintain the changes that they had made to their lifestyles and hoped that this would lead to an improvement in wellbeing and quality of life. In the

DESMOND study there was also no difference in quality of life as measured by the WHOQOL-BREF between the intervention and control arm. However, in the DESMOND study illness understanding was improved in the intervention group, compared to usual care up to three years following the intervention (41). The education programme in the DESMOND study differed from the ACTID programme in that it was delivered in groups and used different psychological theories. In addition, those participants in the control arm in the ACTID study at 12 months received all of the teaching material that had been used in the interventions arms. Any or all of these differences might explain why the DESMOND study was able to show an improvement between their treatment arm and control arm but our trial was not able to.

Our results in treatment satisfaction highlight the importance of increased contact time and the effect of a trial environment on people's satisfaction with the care they receive. The improvement in satisfaction that occurred in all arms over 1 year, which was significantly greater in the intervention arms, was lost as soon as participants left the trial. We believe this shows the beneficial impact taking part in a trial has on the clinical care of participants.

To our knowledge, alongside DPPOS this study is the longest duration study of quality of life in people with newly diagnosed Type 2 DM and has number of strengths. Firstly, there was adequate retention of trial participants with almost half (49%) of participants with baseline data retained at six years. In addition, baseline scores in these measures were similar between those individuals lost at six years and those retained. Secondly, the measures we used all display good reliability and validity. Finally, with the only treatment satisfaction differing between arms and this effect being lost after completion of the trial, we were able to combine all participants into a single cohort to provide increased statistical power to detect changes in these measures.

There are some important limitations to note. As Early ACTID recruited people in whom a diagnosis of Type 2 DM was made 3-8 months previously, we were unable to capture any changes that occur immediately at diagnosis. Secondly, the slight difference in baseline clinical characteristics in those retained and those lost at six years may have influenced our results. Thirdly, participants' involvement in Early ACTID (the majority in intervention arms) may have had a lasting impact, particularly on quality of life and illness perception, as even

those in the control arm received an “enhanced” usual care. This may somewhat reduce the generalisability of our findings to the real world. In addition, in order to analyse our findings based on time of diabetes progression we were forced to categorise our cohort into groups. However, more complex joint modelling with diabetes progression as a survival outcome would better assess this association. Finally, disentangling changes in quality of life due to Type 2 DM and those that occur with ageing and the acquisition of comorbid diseases is not possible from our study. The use of a diabetes-specific measure of quality of life such as ADDQOL in combination with more responsive generic-measures such SF-36, and monitoring of comorbid conditions could aid in doing so.

In summary, we found quality of life in newly diagnosed Type 2 DM declines over six years. This decline was associated with progression of diabetes, particularly within the first year. Future work should ideally take the form of a long duration prospective cohort study to remove the effect of a trial environment. We recommend it uses both disease-specific and generic measures of quality of life. Finally, a concurrent qualitative study on a subset of the cohort may provide insight into the reasons for this decline and how these may be addressed.

Chapter 5 – Discussion

Summary

In this project we investigated treatment satisfaction, quality of life, illness perception, global life satisfaction and self-esteem in the participants of the Early ACTID randomised control trial and its follow up study ACTID Plus.

Chapter 3 looked at the effects of the trial interventions on these constructs and the effects of these constructs on trial outcomes. In Chapter 4 we modelled the longitudinal changes in these constructs over six years. We also assessed any association between these constructs and progression of Type 2 diabetes as defined by increased HbA1c or increased diabetes medication requirement.

We demonstrated in Chapter 3 that diet and diet plus physical activity interventions improved treatment satisfaction in early Type 2 DM. In addition, we showed the interventions had no effect on quality of life, illness perception, life satisfaction and self-esteem. We also demonstrated the addition of physical activity advice to a dietary program did not result in an additional benefit in any of these measures. There was also no association between baseline quality of life, illness perception, life satisfaction or self-esteem and response to the interventions in weight loss or glycaemia.

We demonstrated in Chapter 4 that quality of life declines over the six years following diagnosis of Type 2 DM. This decline was associated with progression of diabetes. In addition, we showed there is a modest decline in perceived illness threat over this time. The benefits in treatment satisfaction shown in Chapter 3 were quickly lost and follow up satisfaction scores quickly returned to their baseline level.

Conclusions

Adherence to lifestyle interventions in Type 2 diabetes is poor. Anecdotally, there has been suggestions that this is due to the fact sticking to diet and physical activity programs can make you unhappy. This is supported by research into the barriers to changing lifestyle that has found dieting to be as great a burden as insulin treatment and identified barriers to exercise such as physical discomfort and stigma, particularly in obese people (23–25). With this in mind, the most important finding of this work was that behavioural lifestyle interventions delivered in newly diagnosed Type 2 diabetes do not result in reduced quality of life, illness perception or psychological wellbeing.

At the time of the Early ACTID trial there had been increasing calls for physical activity to be provided to people with newly diagnosed Type 2 diabetes on a large scale. This would require extensive training of healthcare staff at a huge cost to the NHS. The main findings of Early ACTID refuted these calls as it showed adding physical activity advice to an effective dietary intervention did not confer any additional benefits in glycaemia, insulin resistance, weight loss, or medication requirement (72). The work presented in this thesis adds further weight to this argument by showing there are no benefits in quality of life, treatment satisfaction or wellbeing gained by adding physical activity.

There is concern over whether poor quality of life or psychological wellbeing may lead to poor adherence and response to lifestyle interventions delivered early in Type 2 diabetes. Anecdotally, there is unease among clinicians about asking people who are unhappy or worried to make changes to their lifestyle without first addressing these issues. Previous studies have supported this notion as depression is associated with poorer adherence to lifestyle interventions (56). We were able to address this concern in our study and found baseline levels of quality of life, self-esteem and life satisfaction did not influence response to the interventions. This provides reassurance to clinicians that these interventions can be delivered to everyone, even if they have poorer quality of life or psychological wellbeing. However, we did not look at depression in our study so we cannot infer from our results that the interventions would have remained effective in the context of depression.

We have shown that like studies of various diabetes medications, treatment satisfaction is significantly improved by diet and diet plus physical activity interventions delivered within a trial environment (65). Similar results were also seen in the Diabetes X-PERT study of lifestyle interventions in established Type 2 diabetes (67). In addition to the large improvements seen in the intervention arms, there was also a smaller improvement in the treatment satisfaction of those receiving usual care. The fact these benefits in all arms were lost after participants left the trial highlights the impact improved clinical outcomes and involvement in a trial can often have on an individual's perception of their care.

There is a paucity of evidence of what happens to the quality of life of people with newly diagnosed Type 2 diabetes in the UK. Quality of life is often only investigated in interventional trials, often with short follow up. For this reason, evidence of the change in quality of life that occurs over the first years following diagnosis prior to the development of complications is restricted to one major study. The American DPPOS study found quality of life declines slowly over up to six years following the diagnosis of Type 2 diabetes (38). Applicability of these findings to people with newly diagnosed Type 2 diabetes in the UK is limited by the fact it occurred in a very different healthcare system. They were also a group of people in whom the diagnosis of diabetes had been made despite being made aware of their risk and their best efforts prevent it. We were able to show in this thesis that quality of life does indeed decline slowly over the six years following diagnosis of Type 2 diabetes.

Disentangling whether declining quality of life is due to diabetes or simply related to aging is difficult. Quality of life is known to decline with age and UK population norms for the EQ-5D Index show that health status declines from 0.91 for those aged under 25 to 0.65 for those aged 65-74 (97). The decline we saw of 0.06 over the six years therefore represents a significant drop. Our results suggest that this decline is more likely to be due to diabetes, particularly early on, as those whose disease progressed during the trial experienced the greatest decline in quality of life over the six years.

Another factor that may influence poor adherence to diabetes is a lack of concern for the consequences of the disease, this may in turn lead to quicker progression of the disease. We did not find this as perceived illness threat was not associated with response to interventions or to disease progression.

Perceived illness threat also seems to fall slowly over the six years. This could be explained by people gradually coming to terms with their diagnosis of a chronic illness and its effects on their daily functioning.

Finally, Type 2 diabetes can cause people with the disease to feel shame or stigma and many people blame themselves for developing the disease (98). As a result it can severely impact an individual's self-worth and self-esteem.

Reassuringly, life satisfaction and self-esteem appear to be remarkably stable over this period. This perhaps suggests these psychological constructs are not specifically affected by Type 2 diabetes and may be more associated with obesity that would likely pre-exist the development of diabetes.

Implications

The work contained in this thesis has a number of important clinical implications. The first is that a reduction in quality of life or wellbeing is not the reason for the poor adherence to lifestyle interventions seen in Type 2 diabetes. This means we need to look elsewhere for an explanation for the poor adherence.

Secondly, it seems very intensive programs are required to see improvements in quality of life and wellbeing. The considerable weight loss seen in the intervention arm of the DiRECT randomised control trial of an intensive weight management program for the remission of diabetes was associated with improved quality of life (22). However, the more modest weight loss in Early ACTID was unable to produce an improvement. This adds further to the evidence significant weight loss is required to improve quality of life in obese individuals (87).

The confirmation that there is no additional benefit obtained from adding physical activity advice to dietary advice has far reaching implications. The findings in Early ACTID that both clinical and patient-reported outcomes were no different between a diet and diet plus physical activity intervention provides clear evidence of the lack of benefit. The implication of this is that if we are to improve peoples' diabetes through lifestyle interventions, the NHS should focus on ensuring everyone receives high-quality dietary advice close to diagnosis.

The fact we found those who progressed quickly within the trial period experienced the greatest reduction in quality of life has significant clinical implications. The clinical implication of this finding is that if we are to delay the decline in quality of life seen in the first years of Type 2 diabetes, then early management to delay disease progression is vital. Early intensive dietary interventions therefore not only have the ability to improve clinical outcomes but have the ability to delay and/or prevent a decline in quality of life.

Limitations

There are some limitations to this work. Many of these were unavoidable, particularly as it was carried out on an existing dataset. There are some limitations of the original study design that are worth noting. Due to the nature of the interventions in Early ACTID it was impossible to blind participants, nurses and dietitians to arm allocation which may introduce unwanted biases. This was minimised as much as possible by keeping doctors blinded to arm allocation. Secondly, making comparisons between the intervention arms is limited by the smaller sample size of the usual care arm and the fact that they received slightly better care than they would have received in routine clinical practice. This is a very practical issue. Recruiting and retaining participants in the usual care arm if they did not receive any benefit for their involvement would have been difficult and unethical.

The work in this thesis was also limited by the measures used in Early ACTID. The use of EQ-5D to assess quality of life is limited by the fact some believe it is better described as a measure of health status, as it does not take into account fully an individual's perception of other aspects outside health (33). In addition, it is a generic measure so it makes it more difficult to attribute changes directly to diabetes. Perhaps concurrent use of a diabetes-specific measure of quality of life would have been ideal.

We saw a significant ceiling effect in the DTSQ Satisfaction Scores. This a well-known issue that led to the development of the DTSQ Change version (DTSQc) (88). However, the fact we saw an immediate drop in treatment satisfaction after completion of the trial provides us with reassurance it remained responsive.

Whilst self-esteem and global life satisfaction are important components of psychological wellbeing, the use of a validated measure of depression would have provided important insight into its effect on response to lifestyle interventions and on quality of life. These associations have been reported elsewhere so would be of great interest in this cohort of newly diagnosed Type 2 diabetes (40,56).

The generalisability of our findings is limited by the fact our cohort was not ethnically diverse with 96% Caucasian. In addition, the longitudinal changes we assessed may have been influenced by lasting effects of participants'

involvement in Early ACTID (the majority in intervention arms). Incomplete questionnaire data was a further issue, with just under half of participants (49%) completing at least one questionnaire in full at six years. This was not related to retention of participants as 82% of those who agreed to be followed up were retained after six years, however many of them stopped completing the questionnaires. We also saw some slight differences in baseline clinical characteristics between those retained at six years and those lost to follow up. However, importantly the baseline scores for all of these patient-reported measures were similar between the two groups.

Future work

While this thesis answered a number of important questions regarding quality of life and wellbeing in newly diagnosed Type 2 diabetes there are many further questions that can be answered using this dataset. Modelling of which clinical factors had the greatest effect on quality of life and wellbeing would provide insight into possible areas that could be the focus for improving quality of life and wellbeing in this population. In addition, modelling of the combined clinical and patient-reported outcomes may reveal those factors most important in determining whether an individuals' diabetes progresses or doesn't progress.

Complete evaluation of the association between diabetes progression and each of the measures of quality of life and wellbeing requires complex modelling beyond the scope of this work. Questionnaire data in this study represents multilevel repeated-measures data, and diabetes progression a survival-type binary outcome. Joint modelling allows for simultaneous modelling of the repeated measure and survival outcomes and would provide definitive evidence of any associations between diabetes progression and quality of life or wellbeing (99).

Patient-reported outcomes are rarely the primary outcome of interventional trials. With this in mind, future work on the impact of lifestyle changes in early Type 2 diabetes on quality of life and wellbeing should take the form of a prospective cohort study. Assessing associations between these measures and objectively measured diet and physical activity levels would provide these answers. This would remove the issue of usual care representing an "enhanced" usual care and the possible lasting impact of interventions on the longitudinal change in quality of life and wellbeing seen over the first few years following diagnosis of Type 2 diabetes. It should use a combination of generic and disease-specific measures of quality of life in order to attempt to isolate the effects of diabetes on quality of life. Regarding wellbeing, employing measures of depression and diabetes distress would add further to answering whether psychological wellbeing is associated with differential response to lifestyle changes.

In the field of interventional trials, patient-reported outcome measures are an increasingly important outcome when evaluating new treatments (100). Going

forward it is hugely important for measures used in these trials to be standardised to maximise meta-analysis and cross comparison. The effects on patient reported outcome measures may be small meaning that a meta-analysis may be needed to detect these changes. At the moment, this is very difficult due to the huge variation in patient reported measures used to assess outcomes such as treatment satisfaction, wellbeing and quality of life. Thus, there needs to be agreement as to which of these patient reported measures should be used to assess each specific outcome.

Finally, fundamentally patient-reported outcome measures are limited by the fact that they attempt to quantify cognitive and emotional perceptions that are in essence very qualitative. Although qualitative studies are not feasible or helpful on a large scale, performing concurrent qualitative studies on a subset of study cohorts may help to provide insight into the particular factors affecting quality of life and wellbeing. These results, in combination with both diabetes-specific and generic measures of quality of life, would provide almost definitive evidence of the changes in quality and wellbeing that occur in Type 2 diabetes and its treatment.

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Appendix

Appendix 1: Questionnaires given to participants

Given exactly as participants received the questionnaires.

Wellbeing Questions.

The aim of these questions is to assess how happy you are and how diabetes is affecting your life. Please read the instructions for each section very carefully as the way in which you need to answer the questions varies. If you have any questions please ask the nurse who is conducting the visit.

Wellbeing Questions.

Diener's Satisfaction with Life Questionnaire : *Baseline, 6, 12.*

This is a short, 5-item instrument designed to measure global cognitive judgments of one's lives (global life satisfaction). Below are five statements that you may agree or disagree with. Using the 1 - 7 scale below indicate your agreement with each item by placing the appropriate number in the box preceding that item.

1 - Strongly disagree

2 - Disagree

3 - Slightly disagree

4 - Neither agree nor disagree

5 - Slightly agree

6 - Agree

7 - Strongly agree

In most ways my life is close to my ideal.

The conditions of my life are excellent.

I am satisfied with my life.

So far I have gotten the important things I want in life.

If I could live my life over, I would change almost nothing.

Rosenberg Self-Esteem Scale : *Baseline, 6, 12.*

Below are five statements that you may agree or disagree with. Using a scale of 1 - 4 indicate your agreement with each item by placing the appropriate number in the box preceding that item.

(1 = strongly agree, 2 = agree, 3 = disagree, 4 = strongly disagree)

On the whole I am satisfied with myself

At times I think I am no good at all

I feel I have a number of good qualities

I am able to do things as well as most others

I feel I don't have much to be proud of

I certainly feel useless at times

I feel I am a person of worth, at least on a plane with others

I wish I could have more respect for myself

All-in-all, I'm inclined to feel that I'm a failure

I take a positive attitude toward myself

EQ5D - Baseline, 6, 12.

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

- ☐ I have no problems in walking about
- ☐ I have some problems in walking about
- ☐ I am confined to bed

Self-care

- ☐ I have no problems with self-care
- ☐ I have some problems washing or dressing myself
- ☐ I am unable to wash or dress myself

Usual activities (e.g. work, study, housework, family or leisure activities)

- ☐ I have no problems with performing my usual activities
- ☐ I have some problems with performing my usual activities
- ☐ I am unable to perform my usual activities

Pain/Discomfort

- ☐ I have no pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have extreme pain or discomfort

Anxiety/Depression

- ☐ I am not anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am extremely anxious or depressed

Valuing your own health today.

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate how on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own
health state

*Best
imaginable
health state*

100

90

80

70

60

50

40

30

20

10

0

*Worst
imaginable
health state*

DIABETES TREATMENT SATISFACTION QUESTIONNAIRE (DTSQ)

The following questions are concerned with the treatment for your diabetes (including insulin, tablets and diet) and your experience over the last few weeks. Please answer each question by circling a number on each of the scales.

1. How satisfied are you with your current treatment?

very satisfied 6 5 4 3 2 1 0 very dissatisfied

2. How often have you felt that your blood sugars have been unacceptably high recently?

most of the time 6 5 4 3 2 1 0 none of the time

3. How often have you felt that your blood sugars have been unacceptably low recently?

most of the time 6 5 4 3 2 1 0 none of the time

4. How convenient have you been finding your treatment to be recently?

very convenient 6 5 4 3 2 1 0 very inconvenient

5. How flexible have you been finding your treatment to be recently?

very flexible 6 5 4 3 2 1 0 very inflexible

6. How satisfied are you with your understanding of your diabetes?

very satisfied 6 5 4 3 2 1 0 very dissatisfied

7. Would you recommend this form of treatment to someone else with your kind of diabetes?

Yes, I would	6	5	4	3	2	1	0	No, I would definitely
				definitely not				
recommend the								recommend the
treatment								treatment

8. How satisfied would you be to continue with your present form of treatment?

very satisfied 6 5 4 3 2 1 0 very dissatisfied

Please make sure that you have circled one number on each of the scales.

The following questions look at how you perceive your diabetes, please circle the number that best corresponds to your views:

0 1 2 3 4 5 6 7 8 9 10
no affect at all severely affects my life

[illegible]

0 1 2 3 4 5 6 7 8 9 10

absolutely no controlextreme amount of control

0 1 2 3 4 5 6 7 8 9 10
not at all extremely helpful

0 1 2 3 4 5 6 7 8 9 10
no symptoms at all many severe symptoms

0 1 2 3 4 5 6 7 8 9 10
not concerned at all extremely concerned

0 1 2 3 4 5 6 7 8 9 10
don't understand at all understand very clearly

0 1 2 3 4 5 6 7 8 9 10
not at all affected emotionally extremely affected emotionally

Please list in rank-order the three most important factors that you believe caused your illness. *The most important causes for me:-*

1. _____

2. _____

3. _____